THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 168, NO. 10 — CHICAGO, ILLINOIS — NOVEMBER 8, 1958

COPYRIGHT, 1958, BY AMERICAN MEDICAL ASSOCIATION

DIAGNOSIS OF PERIPHERAL ARTERIAL EMBOLI OF THE EXTREMITIES

John T. Phelan, M.D.
and
William P. Young, M.D., Madison, Wis.

The clinical features of an acute peripheral arterial embolus are considered to be a rigidly fixed series of events, namely, sudden, abrupt, excruciating pain followed by numbness, pallor of the extremity, and absent pulsations. However this sequence of events may be the exception rather than the rule, inasmuch as the onset of pain may be insidious and, in some instances, preceded by paresthesias of the involved extremity. In many instances the diagnosis of a peripheral arterial embolus depends on the assessment of minor signs and symptoms. Next to pain, the vascular disturbances manifested by absent arterial pulsations and color and temperature changes in the involved extremity are prominent features of an acute arterial occlusion. The frequent association of cardiac abnormalities with peripheral arterial embolus should be well known. In addition there is a prevalence of emboli involving the femoral artery.

RECENT observations by a number of authors have shown that early diagnosis of a peripheral arterial embolus, followed by its surgical removal with restoration of blood flow whenever possible, will, in most instances, be superior to conservative measures in terms of patient mortality and morbidity.[1] Furthermore, accumulative clinical data have suggested that surgical treatment is most effective when employed within the first 24 hours after lodgment of the embolus. However, in most reported series,[1] a large percentage of the patients have presented signs and symptoms for at least 24 hours or longer before surgical attention was considered; in this regard, our series is no exception. In evaluating this problem, we found a certain number of patients who had disease conditions that were considered at the time to be contraindications to surgical removal of the embolus. Still, in a number of cases the atypical clinical course suggested to the attending physician a condition other than an acute arterial occlusion. Hence, surgical intervention was delayed, and, in most instances, the patient presented ischemic changes of an irreversible nature at the time of surgical evaluation.

Because of this problem, this report concerns a clinical review of patients seen with peripheral arterial emboli of the extremities at the University Hospitals, with particular attention given to the signs and symptoms of this condition and emphasis on early diagnostic criteria.

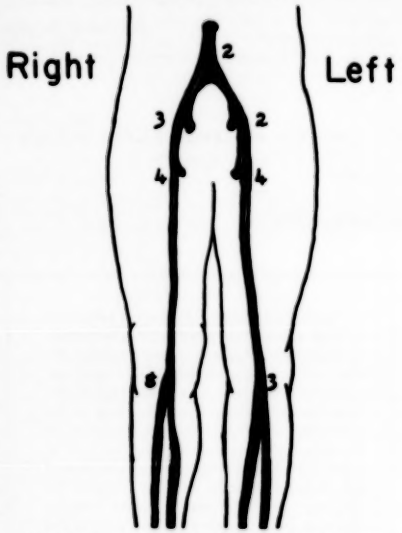
From the Department of Surgery, University Hospitals, University of Wisconsin School of Medicine.

From June, 1951, to January, 1957, inclusive, the diagnosis of peripheral arterial emboli involving the upper and lower extremities was made in 30 patients. Data gleaned from a critical review of the clinical records of these patients constitute the basis of this report.

The youngest patient in our series was 39 years of age, while the oldest was 79. The average age of the patients in this group was 62.

Etiology

In most collected series of this nature [2] cardiac conditions manifested by auricular fibrillation, mitral valvular disease, and recent myocardial infarction have been found primarily responsible for the



Sites of lodgment of emboli in 26 patients with acute peripheral arterial occlusion (in four instances upper extremity was involved).

etiology of the embolus. Our findings were quite similar, and to present them in detail would only be a repetition of a known fact. However, in five instances chronic congestive heart failure was the only cardiac finding, a point that has been afforded little emphasis with respect to the etiology of a peripheral arterial embolus. Unmistakable clinical evidence of cardiovascular disease was present in 29 of the 30 patients. Particular diagnoses included auricular fibrillation, 19; congestive heart failure, 5; mitral valvular disease, 3; and myocardial infarction, 2. In only one case was the acute arterial occlusion considered to be a primary thrombosis.

Location and Symptoms

Location.—The sites of lodgment of the emboli, as determined by physical examination, surgical arterectomy, and autopsy examinations, are shown in the figure. The prevalence of emboli involving the femoral artery is to be noted.

Symptoms.—Pain heralded the onset of a peripheral arterial embolus in 24 of the 30 cases. In five instances the embolic event was manifested initially by paresthesias of the extremity, while one patient experienced a weakness of the involved limb as the initial symptom.

Twenty-four of the 30 patients presented a combination of two or more of these subjective symptoms, namely, pain, followed by paresthesia (numbness, coldness, tingling, and heaviness), and/or paralysis.

The 24 patients whose initial symptom was pain described this sensation under a variety of terms which ranged from excruciating pain to simply a mild ache. In 18 instances the pain was abrupt and sudden and was frequently described as severe or excruciating in character. Although our records are incomplete, it was suggested that such pain manifested itself in one or two ways: either it was localized initially to specific regions of the extremity, namely, foot, hand, calf, popliteal space, or groin, or, less frequently, it involved the entire limb. Furthermore, its duration was variable, for, in some cases, it persisted for three to four hours and in one case less than one hour, only to be replaced by a numb distressful feeling to the limb. Still others noted the pain to be continuous and to involve the entire limb during the first 24 hours. It was also our impression that in some cases the character of the acute pain gradually subsided, only to be replaced by an ischemic, neuropathic type of pain.

As previously stated, six patients noted the onset of pain to be insidious in nature and most frequently described it as an aching sensation. In one case the entire limb was involved, while the remaining five patients indicated the site to be either the foot or the region below the knee. Four patients noted the pain to increase in intensity and severity during the first 24 hours; the other two patients noted little increase in its intensity except when the limb was exercised. It was of interest that each of these six patients complained of coldness of the involved extremity.

Paresthesia.—Eighteen patients in this series experienced some type of paresthesia. In 10 cases it was described as numbness and in 7 as coldness of the extremity; these two subjective sensory complaints were present in combination in nine instances. In addition, tingling, burning, and heaviness of the involved limb were noted by three patients. As previously stated, in five patients the above sensory disturbances were the initial complaint referable to a peripheral arterial embolus. In three instances pain followed and was mild in two

patients and severe in another, and, in each case, it persisted for at least 24 hours; in two patients, the pain was not felt until the limb was exercised and intermittent claudication was noted.

Motor Findings.—In six instances, paralysis of the involved extremity or a specific group of muscles was observed. In five cases the motor changes followed other subjective symptoms; however, in one case its presence was the first evidence of an acute arterial occlusion. The onset of muscular paralysis was variable, and in one patient it was apparent within 10 minutes after the embolic episode. In one case the entire extremity was completely paralyzed, while in the remaining five patients only the foot and toes were involved. In no instance were the motor findings transient, but once they made their appearance they became permanent unless the ischemia was relieved.

As many of our patients were seen hours or days after their embolic event, signs of advanced ischemia were unmistakably evident. However, in seven instances the interval between onset and hospital admission was less than six hours, and in four the acute arterial embolus occurred during the patient's hospitalization for some other condition. From this group, certain definite observations were available. First, in four patients, pallor of the extremity was the initial color change and, in time, (the earliest within 30 minutes, the longest 24 hours) cyanosis was recorded in the initial color change. In four instances the color change was manifested by a visible line of demarcation at the knee level. In three patients the foot and ankle presented this phenomenon.

Second, a temperature difference was distinguished in each patient, which corresponded with the color change. In three patients this difference was more diffuse and extended beyond the color line.

Comment

The clinical features of an acute peripheral arterial embolus are considered to be a rigidly fixed series of events, namely, sudden, abrupt, excruciating pain followed by numbness, pallor of the extremity, and absent pulsations. However, as indicated by the data presented here, this sequence of events may be the exception rather than the rule, inasmuch as the onset of pain may be insidious and, in some instances, preceded by paresthesias of the involved extremity. Moreover, in one of our patients, motor weakness of a specific group of muscles was the first indication that an acute peripheral arterial embolus had taken place. These observations are not original, as a number of authors have recorded similar findings; however, their importance as diagnostic criteria of an arterial embolus has not received due emphasis.

For example, Allen and his associates,[3] at the Mayo Clinic, reported that only 48% of patients in their series experienced an abrupt onset of symptoms. This figure corresponds closely to that given by Haimovici,[2] who found sudden pain to be the principal clinical feature in only 60% of the patients in his series of 330 cases of embolism, and by Richards,[4] who found that 11 of his 48 patients experienced symptoms other than acute pain. Our own experience is quite similar, for of the 30 cases of peripheral arterial emboli the onset of symptoms was abrupt in 18. In five patients numbness of the extremity replaced pain as the dominant symptom, and in six pain was the first symptom; however, its character was not the intense, sudden, agonizing pain one frequently associates with this condition. This factor accounted for delayed diagnosis in the great bulk of these cases seen in this series.

This atypical clinical symptomatology in some cases of peripheral arterial emboli is difficult to explain, since analysis of our cases indicates this feature was not related to age or location of the embolus. Richards [4] has discussed this problem quite succinctly in a recent paper and relates that Lewis, in 1936, considered the pain of an acute arterial occlusion to be directly related to the degree of muscle ischemia. However, the variance of this one symptom has suggested to Richards that muscle ischemia is not the sole underlying mechanism. He believes that dilation of the artery by the embolus may be an additional and principal factor in explaining the sudden onset of pain and its localization to a specific part of the extremity. Furthermore, he indicates that this dilating component may be absent and the artery lumen only partially occluded in those cases where the pain is slowly progressive or is preceded by paresthesias of one type or another. Still others tend to link the appearance of acute pain with arterial spasm, a factor Richards believes has received more emphasis than it rightly deserves in the etiology of pain in an acute arterial occlusion.

Next to pain, the vascular disturbances manifested by absent arterial pulsations and color and temperature changes in the involved extremity are prominent features of an acute arterial occlusion. In our series, we found pallor of the extremity to be an early event and this was followed by cyanosis of the involved limb. In addition, the finding of absent, or diminished, arterial pulsation was, in each instance, accompanied by color and temperature change.

The frequent association of cardiac abnormalities with peripheral arterial embolus is a well-known fact, and in our series such was the finding in 29 of the 30 patients. Hence, the presence of auricular fibrillation, mitral valvular disease, recent myocardial infarction, and congestive heart failure are so closely allied with this condition that their presence alone in patients who present atypical motor and sensory disturbances to one or more extremities should suggest the presumptive diagnosis of an arterial embolus until proved otherwise.

Summary

In one-third of 30 cases of acute peripheral arterial occlusion, the onset of symptoms, principally pain, was insidious and, in some instances, paresthesias preceded the latter as the chief symptom. In the remaining cases the abrupt onset of pain was characteristic; however, its duration and behavior were uncertain. These findings suggest that in many instances the diagnosis of a peripheral arterial embolus will depend on the assessment of minor signs and symptoms, a concept that is in contrast to the usual expectation of an acute artery occlusion, namely, a sudden, painful, dramatic event.

1300 University Ave. (6) (Dr. Phelan).

References

1. Rosenberg, J. C.; Emerson, E. C.; and Murphy, T. O.: Clinical Study of Embolectomy, Angiology 8:371-377 (Oct.) 1957. Shumacker, H. B., and Jacobson, H. S.: Arterial Embolism, Ann. Surg. 148:145-152 (Feb.) 1957. Warren, R., and Linton, R. R.: Treatment of Arterial Embolism, New England J. Med. 238:421-429 (March 25) 1948. Warren, R.; Linton, R. R.; and Scannell, J. G.: Arterial Embolism: Recent Progress, Ann. Surg. 140:311-317 (Sept.) 1954.

2. Haimovici, H.: Peripheral Arterial Embolism: Study of 330 Unselected Cases of Embolism of Extremities, Angiology 1:20-45 (Feb.) 1950.

3. Allen, E. V.; Barker, N. W.; and Hines, E. A., Jr.: Peripheral Vascular Diseases, Philadelphia, W. B. Saunders Company, 1955, pp. 180-197.

4. Richards, R. L.: Effects of Peripheral Arterial Embolism, Quart. J. Med. 23:73-90 (Jan.) 1954.

PREVENTION OF URINARY CALCULI AFTER PARALYTIC POLIOMYELITIS

Fred Plum, M.D., Seattle

Prophylaxis of urinary lithiasis is an important part of the management of patients with paralytic neurological diseases. The development of urinary calculi may otherwise produce as much disability, or more, than that caused by the paralysis itself.[1] Several analyses indicate that patients severely paralyzed by poliomyelitis frequently develop calcium phosphate urinary calculi. Calculi were found in 33 (33.7%) of 98 long-term and in 1 of 32 short-term respirator patients by Taylor, Alcock, and Hildes.[2] No stones were present in 112 nonrespirator patients with spinal paralysis. Slotkin, Loeser, and Ament [3] reported renal stones in 19 (40.4%) of 47 consecutive respiratory patients. Rodgers, Ellwood, and Ratelle [4] noted that 22 (33%) of 66 adult respirator patients and 8 (31.6%) of 25 children in respirators developed stones. Calculi were found only twice in nonrespirator patients with spinal paralysis. Affeldt [5] detected renal calculi in 14.9% of 675 convalescent patients at the Rancho Los Amigos Respiratory Center. The incidence rose to 23% in the 338 patients over 20 years of age.

Urinary calculi after poliomyelitis are largely confined to long-term respirator patients. Prophylaxis of calculi can be effective if begun early in the paralyzing and immobilizing diseases. Proper positioning is required to prevent stasis of crystalline material in the genitourinary tract. Calcium intake of 500 to 700 mg. daily was achieved by limiting milk and milk products to the equivalent of one and one-half glasses. Having patients produce 1,500 to 2,000 ml. of urine daily is the hardest task in the prophylactic program. Placing fluid reservoirs, connected to self-service drinking tubes, next to each patient aided in attaining a high fluid intake. The medical problem of renal stones was discussed frequently in lay language with the patients as a group. Once the problem was understood by some of the patients, one or more usually prompted the rest to work toward the required fluid volumes. A program of prophylaxis of urinary calculi appears to be widely applicable.

Pathogenesis

Hypercalciuria and Hyperphosphaturia.—Skeletal demineralization with hypercalciuria and hyperphosphaturia almost invariably follows paralytic poliomyelitis.[6] Hypercalciuria, in the immediate weeks after the onset of poliomyelitis, tends to be intense in both mildly and severely paralyzed patients. Subsequently, the duration of hypercalciuria is proportional to the degree of paralysis, and an increased urinary calcium content may continue for 6 to 12 months or more in patients with paraplegia or quadriplegia.[6b] Artificial mobilizing procedures have little effect on the intensity or duration of the calcium losses.[7]

Well-controlled studies on the effects of dietary calcium on urinary calcium excretion are limited. Howard, Parson, and Bigham [8] noted only inconse-

From the Department of Medicine, Division of Neurology, University of Washington School of Medicine.

Read before the Section on Nervous and Mental Diseases at the 107th Annual Meeting of the American Medical Association, San Francisco, June 27, 1958.

quential changes in the urinary calcium of patients with fractures after large shifts in dietary calcium. However, Dunning and I[7] observed a rise in the serum calcium from 11.8 to 13.1 mg. per 100 cc. within two weeks in a boy with paraplegia due to poliomyelitis when the daily calcium intake was raised from 0.5 Gm. to 1.5 Gm.

Reduced Urine Flow.—Hypercalciuria and hyperphosphaturia increase the amount of urinary solutes. Diminished fluid intake due to a combination of anorexia and increased insensible water losses may decrease the renal clearance of water at the same time. A further rise in urinary solute concentration results.

Urinary Tract Infection.—Many poliomyelitis patients require catheterization to drain transiently paralyzed bladders. Few escape infection with urea-splitting bacteria after this procedure; an alkaline urine results, in which calcium phosphate can exceed its solubility constant and precipitate as apatite and struvite.[9] Infection also creates both denuded areas of urinary tract mucous membrane and exudates of organic material which may provide the matrix for stone formation.[10] It has been noted previously that stones that appear after poliomyelitis are apt to be restricted to patients with urinary tract infection.[11]

Stasis.—The posterior renal calyces fail to drain by gravity except when the patient is in the prone or erect position.[12] Hence, in recumbent immobilization any material which precipitates in the urine tends to drift into and remain stagnant in the dependent calyces. The combination of an increased calcium phosphate excretion, decreased urinary flow, a urine pH favoring precipitation of crystalline material, a readily available organic detritus for matrix formation, and stagnant regions from which drainage is limited creates a formidable risk of calculi. Other factors, such as the respiratory alkalosis which results from chronic respirator treatment,[13] may contribute to this risk.

Prophylaxis

Clinical Material.—This study was initiated at the New York Hospital in 1949 and continued from 1953 until the present at the Northwest Respirator and Rehabilitation Center of the University of Washington, Seattle. Of the 500 or more patients with poliomyelitis admitted to the two institutions, there were 115 with extensive paralysis who were under direct observation for periods lasting six months or more. Forty-one were at the New York Hospital and the remainder were treated in Seattle.

Twenty-five patients had severe paralysis of the trunk and extremities (total paraplegia, triplegia, or quadriplegia) without requiring respirator care. Twenty extensively paralyzed subjects required short-term (six weeks or less) treatment in the respirator, and 69 other extensively paralyzed patients required long-term (more than six weeks) respirator treatment. Among the respirator patients, 55 were under our supervision during both the acute and convalescent stages of poliomyelitis. Measures designed to prevent the development of urinary calculi were carried out in these 55 patients throughout their entire illness. This will be referred to as the "early treated" group. Thirty-four respirator patients were transferred to us from other hospitals for rehabilitation care at intervals ranging from two months to three years after the onset of poliomyelitis. These patients had not previously been on a program particularly designed to prevent renal calculi and were designated the "late treated" group.

Treatment Program.—Patients on this service were maintained on a low calcium intake, between 500 and 700 mg. daily. Fluids were forced to produce a measured urinary output of 1,500 to 2,000 ml. of urine per day. Urinary tract infections were treated promptly. All patients, including those in respirators, were turned from side to side several times daily and placed prone as early in convalescence as possible. Rarely was prone positioning delayed longer than four weeks after the onset of treatment. Seven respirator patients, three in the early treated group and four in the late treated group, received norethandrolone (Nilevar) during a metabolic study of this agent.[14] No specific metabolic measures were employed to influence the solute excretion in the other patients. Each patient underwent a general program of convalescent care and rehabilitation and was mobilized as rapidly as his disability permitted.

Detection of Calculi.—Several methods were used to detect urinary calculi. Every patient was under direct clinical surveillance in the hospital for an average of six months during rehabilitation therapy. Periodic x-rays of the abdomen to show calcification in the kidneys, ureters, and bladder were taken on each patient, particularly prior to discharge from the hospital. In addition, all of the patients studied at the Northwest Respirator Center had intravenous pyelograms. Clinical follow-up by questionnaire to determine the incidence of late urinary complications was accomplished in 1954 on 33 of the 41 New York Hospital patients. Either direct clinical and x-ray follow-up or a follow-up through the current attending physician has been achieved for an average of three years to date on all of the Northwest Respirator Center patients.

Incidence of Urinary Calculi.—The table summarizes the extent of paralysis and incidence of calculi. Urinary lithiasis was detected in respirator-treated patients only, and renal calculi were limited to those patients who had been in respirators for more than six weeks. The figure diagrams the relationship between calculi and the age and sex of the respirator-treated patients.

Three early treated respirator patients developed calculi, an incidence of 5.5%. One boy had a large right renal calculus necessitating surgical removal of both stone and kidney at another hospital two years after the onset of poliomyelitis. One young woman first showed tiny calcifications in the region

of the right renal pelvis two years after the onset of poliomyelitis. The early care of both these patients had been hampered by great difficulties in changing them from the recumbent position. Their treatment had not otherwise differed from the rest of the early treated group. The third early treated patient with urinary lithiasis developed several small bladder calculi after eight months of indwelling catheterization. She had lumbosacral sensory loss and bladder paralysis associated with acute poliomyelitis.[15] After removal of the bladder calculi by transurethral crushing and a partial resection of the internal urethral sphincter, she has had no other urinary problems for two ensuing years.

Extent of Paralysis and Incidence of Calculi Among 115 Patients

	Patients, No.	With Calculi, No.
Severe spinal paralysis only	25	0
Short-term respirator		
treated early	14	1
treated late	6	0
Long-term respirator		
treated early	41	2
treated late	28	9
Total, early treated respirator cases	55	3(5.5%)
Total, late treated respirator cases	34	9(26.5%)

Nine (26.5%) of the 34 late treated respirator patients developed calculi, eight in the kidneys and one in the bladder. Large stones in the renal calyces and pelves were present in five late treated patients. These calculi were successfully removed surgically in three patients while symptoms were controlled by conservative treatment in the other two who were precarious surgical risks. The calculi in three late treated patients were asymptomatic and detected only as small radiopaque densities in the region of the renal calyces. One late treated patient showed several small bladder calculi which necessitated transurethral removal. He had had an indwelling catheter for six weeks during his acute illness and early convalescence.

All 12 patients with established calculous disease had been catheterized during acute poliomyelitis and all had persistent bacilluria with organisms of the coli-aerogenes group. Catheterization had also been performed during acute illness in most of the other respirator patients; the majority had bacilluria with gram-negative organisms at some time during convalescence.

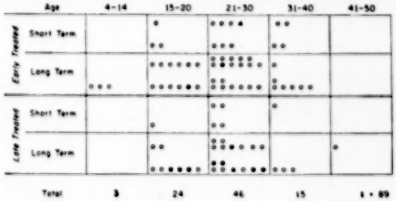
The care of the late treated patients during the first few weeks or months after poliomyelitis differed in several respects from the prophylactic program established for the 55 patients treated from onset of poliomyelitis. Reference to the clinical notes and interviews with the patients indicated that a minority of the late treated patients had been on a restricted calcium intake. Several, including one young woman who showed diffuse renal calcinosis within eight weeks after the onset of poliomyelitis, had had generous milk shake and ice cream supplements. No emphasis had been placed on a high urine output. Few of the late treated patients had been changed from the recumbent position either during their acute illness or in early convalescence and several had been supine for months. However, most of the late treated patients had received appropriate antibiotics for urinary tract infections.

Comment

This study confirms the fact that urinary calculi after poliomyelitis are largely confined to long-term respirator patients.[2] Two of 55 early treated respirator patients and 8 of 34 late treated respirator patients had renal calculi. This contrast in renal stone incidence was striking and indicates that prophylaxis of calculi can be effective if begun early in the paralyzing and immobilizing diseases.

The excellent cooperation of nurses and dietitians made the prophylactic treatment program possible. A calcium intake of 500 to 700 mg. daily was achieved by limiting milk and milk products to the equivalent of one and one-half glasses. Milk products were reduced further when large amounts of fruit juices were taken, since the latter contained approximately 8 mg. of calcium per 100 cc. Extra milk shakes, ice cream, cheese, and milk-base eggnogs were foregone until the expected duration of postparalytic hypercalciuria had passed. This was never less than six months after onset of poliomyelitis.

Having patients produce 1,500 to 2,000 ml. of urine daily was the hardest task in the prophylactic program. Orders to "force fluids" were no guarantee that dilute urines would result, so output measurements were checked frequently. The patients had large insensible water losses, particularly in warm weather, and moderate anorexia often impeded thirst. The extensive paralysis suffered by these patients meant that an attendant was ordinarily required to administer fluids and to empty urinals. Both the patients and the attendants found this irksome. (An example may illustrate some of the difficulties: If a patient takes half a glass of liquid



Incidence of calculi among short-term and long-term respirator patients according to age and sex of patient. Filled triangle = bladder calculus, filled circle = renal calculus, and open circle = no calculi.

Top line in each square indicates women, bottom lines, men.

at each feeding and requires a 3,800 ml. intake to maintain an 1,800 ml. output, 38 separate daily trips by nursing staff are required for fluid intake alone.)

The problems in attaining a high fluid intake were met in several ways. Much of the nursing time required was eliminated by placing fluid reservoirs, connected to self-service drinking tubes, next to each patient. These reservoirs were attached to respirators when necessary. The medical problem of renal stones was discussed frequently in lay language with the patients as a group. Once the problem was understood by some of the patients, one or more usually prompted the rest to work toward the required fluid volumes. The fluid intake was supplemented by intravenous infusions if persistent anorexia or nausea prohibited adequate gastrointestinal ingestion. It was rarely necessary to resort to parenteral routes except during intercurrent infections.

Another purpose behind forcing fluids was to minimize the severity of urinary tract infections. Patients with positive urine cultures were treated for limited periods by specific antibiosis after in vitro sensitivity testing. These measures usually controlled the clinical manifestations of infection, but persistent bacilluria was frequent. Prophylactic or prolonged antibiosis was not employed. Infections with drug-resistant organisms were treated by an increased fluid intake. Efforts to change the urine pH by drugs or diet were met with only limited success.

After the third month of convalescence, those patients with calculi had frequent urinary tract infections. Acute urinary tract infections after the sixth month of convalescence were reported on follow-up examination by only four patients, who had no demonstrable calculi. In contrast, 8 of the 12 patients with calculi gave histories of either periodic dysuria, flank pain, or acute episodes of pyelocystitis occurring repeatedly in convalescence.

Proper positioning to prevent stasis of crystalline material in the genitourinary tract required considerable efforts by nurses, particularly for patients in respirators. Nonrespirator patients were turned to the prone position at least once daily throughout both acute and convalescent illness. The patients in body respirators were transferred to rocking beds early in convalescence and most could be placed prone shortly afterwards. Passive standing on a tilt table was also employed for many patients to induce gravitational drainage of the kidneys.

Some late treated patients who had remained supine for several months after the onset of poliomyelitis had untoward reactions when changed from the recumbent position. When first placed prone, they passed macroscopic urinary concretions of calcium phosphate salts, producing both pain and hematuria. These complications were minimized by inducing a high urine output for several days before starting prone positioning.

The present study reaffirms the importance of interrupting recumbency to prevent urinary calculi in paralyzed and immobilized patients. There was no way of telling how much protection was added by the other treatment measures. Both of the early treated patients who developed calculi suffered from unusually severe immobilization in the supine position during the first part of their illness. Henceforth, such severely immobilized patients will be treated with testosterone-estrogen combinations or with norethandrolone. These hormones ameliorate hypercalciuria [16] and their addition to the regimen may add some protection for patients in whom recumbency is unavoidably prolonged. However, the low incidence of stones among early treated patients whose position in bed could be changed indicates that special hormones or drugs [17] are unnecessary to protect the majority of appropriately treated paralyzed patients. Other paralyzing and immobilizing diseases produce metabolic changes similar to those which follow poliomyelitis.[18] Therefore, this program of prophylaxis of urinary calculi appears to be widely applicable.

Summary

The incidence of urinary calculi was determined in 115 patients severely paralyzed and immobilized by poliomyelitis. Calculi developed only in respirator patients and were rare unless respirator treatment had been continued for six weeks or more.

A program of prophylaxis of urinary lithiasis was employed which included limiting the calcium intake, insuring a large urine output, promptly and briefly treating urinary tract infections, and minimizing urinary stasis by not allowing patients to remain in the recumbent position for long periods. These measures were initiated within the first month of illness on 55 respirator patients, 3 (5.5%) of whom subsequently developed urinary stones. Initiation of the prophylactic measures was delayed for two months to three years after poliomyelitis in 34 other respirator patients. Nine (26.5%) of this latter group developed calculi.

The effectiveness and simplicity of this regimen for protection against urinary calculi gives it wide applicability in the treatment of patients suffering from paralyzing and immobilizing diseases.

This study was aided by an annual grant from the National Foundation for Infantile Paralysis to the Northwest Respirator and Rehabilitation Center and a grant from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service.

References

1. Berns, S. H.; Lowman, E. W.; Rusk, H. A.; and Covalt, D. A.: Spinal Cord Injury—Rehabilitation Costs and Results and Follow-up in 31 Cases, J.A.M.A. **164**:1551-1558 (Aug. 3) 1957.

2. Taylor, J. R.; Alcock, A. J. W.; and Hildes, J. A.: Urinary Tract Calculi in Poliomyelitis, Canad. M.A.J. **75**:29-34 (July 1) 1956.

3. Slotkin, E. A.; Loeser, W. D.; and Ament, R.: Urological Surgery in Tetraplegic Patients with Respiratory Paralysis, J. Urol. **76**:499-507 (Nov.) 1956.

4. Rodgers, R. S.; Ellwood, P. M.; and Ratelle, A. E.: Urological Complications of Poliomyelitis, J. Urol. **76**:447-452 (Oct.) 1956.

5. Affeldt, J. E.: Personal communication to the author.

6. (*a*) Whedon, G. D., and Shorr, E.: Metabolic Changes in Paralytic Acute Anterior Poliomyelitis: II. Alterations in Calcium and Phosphorus Metabolism, J. Clin. Invest. **36**:966-981 (June, pt. 2) 1957. (*b*) Dunning, M. F., and Plum, F.: Hypercalciuria Following Poliomyelitis: Its Relationship to Site and Degree of Paralysis, A. M. A. Arch. Int. Med. **99**:716-731 (May) 1957.

7. Plum, F., and Dunning, M. F.: Effect of Therapeutic Mobilization on Hypercalciuria Following Acute Poliomyelitis, A. M. A. Arch. Int. Med. **101**:528-536 (March) 1958.

8. Howard, J. E.; Parson, W.; and Bigham, R. S., Jr.: Studies on Patients Convalescent from Fracture: III. Urinary Excretion of Calcium and Phosphorus, Bull. Johns Hopkins Hosp. **77**:291-313 (Oct.) 1945.

9. Elliot, J. S.; Quaide, W. L.; Sharp, R. F.; and Lewis, L.: Mineralogical Studies of Urine: Relationship of Apatite, Brushite, and Struvite to Urinary pH.; J. Urol., to be published.

10. Eisenstaedt, J. S.: Certain Tangible Factors in Etiology of Urinary Calculus, Surg. Gynec. & Obst. **53**:730-734 (Dec.) 1931.

11. References 2 and 4.

12. Joly, J. S.: Stone and Calculous Disease of Urinary Organs, St. Louis, C. V. Mosby Company, 1929.

13. Thompson, A. E.: Electrolyte Studies in Respiratory Paralysis of Poliomyelitis, Am. J. Med. **22**:549-560 (April) 1957.

14. Plum, F., and Dunning, M. F.: Amelioration of Hypercalciuria Following Poliomyelitis by 17-ethyl, 19-nortestosterone (Nilevar), J. Clin. Endocrinol. **18**:860-871 (Aug.) 1958.

15. Plum, F.: Sensory Loss with Poliomyelitis, Neurology **6**:166-172 (March) 1956.

16. Whedon, G. D., and Shorr, E.: Metabolic Studies in Paralytic Acute Anterior Poliomyelitis: IV. Effects of Testosterone Propionate and Estradiol Benzoate on Calcium, Phosphorus, Nitrogen, Creatine and Electrolyte Metabolism, J. Clin. Invest. **36**:995-1033 (June, pt. 2) 1957. Reference 14.

17. Vagelos, P. R., and Henneman, P. H.: Effect of Sodium Phytate on Hypercalciuria of Acute Quadriplegia due to Poliomyelitis: Preliminary Report, New England J. Med. **256**:773-776 (April 25) 1957.

18. Reference 7, bibliography.

EXAMINATION FOR MUSCLE WEAKNESS IN INFANTS AND SMALL CHILDREN

Ernest W. Johnson, M.D., Columbus, Ohio

The diagnosis of suspected muscle weakness in infants up to the age of five years is difficult unless one uses a systematic approach. The steps in the examination are (1) palpation of the muscles, (2) examination for muscle tightness, and (3) demonstration of muscle function. Palpation not only reveals tenderness but also distinguishes among conditions that affect the consistency of the muscle mass. Tightness may be seen in either the affected muscles or their antagonists during passive movements. To observe the function of individual muscles calls for much special maneuvering and close observation. Even after the child supposes the examination to be over, the movements of its arms during the act of dressing afford indications as to the status of the deltoid and other muscles of the upper extremity. Electrodiagnostic methods can prove helpful. These methods of differential diagnosis are essential to proper treatment, since they may decide, as in the case history here cited, between such conditions as poliomyelitis and polymyositis.

Frequently the practicing physician is faced with the difficult problem of examining an infant or small child with suspected muscular weakness. The experience can be less frustrating if one uses a systematic approach to the examination. A review of the current pediatric-neurological literature demonstrates the need to present a relatively simple routine for such an examination. No claims for originality are made for any of the techniques outlined; however, these methods were all developed during two years of observation of, and experience with, the diagnosis and management of muscle weakness problems in a pediatric setting.

Emphasis of this paper will be on detecting muscle weakness in those conditions affecting the motor unit, that is, the lower motor neuron and all the muscle fibers which it innervates. Poliomyelitis has been one of the common clinical conditions affecting the motor unit in children. Others include brachial plexus and nerve injuries at birth, infectious polyneuritis, progressive spinal atrophy of infancy, amyotonia congenita, muscular dystrophy, polymyositis, and postnatal nerve injuries of various

From the Division of Physical Medicine and Rehabilitation, Department of Medicine, Ohio State University, and the Regional Respirator Center, Children's Hospital.

Read before the Section on Physical Medicine at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

types. Upper motor neuron disorders can result in clinical weakness which may be demonstrated by the described techniques, although spasticity and reflex changes, among other neurological signs, are usually more important as diagnostic aids.

The techniques which are used represent attempts to determine whether motor weakness can be detected in specific muscle groups. When the presence and distribution of muscle weakness is determined, then additional diagnostic procedures can be undertaken.

The steps in the examination are as follows: (1) palpation of the muscle bellies; (2) examination for muscle tightness; and (3) demonstration of muscle function (with separate consideration for the infant and the walking child).

The only requirements for the examiner are a working knowledge of functional anatomy and acquaintance with the motor development of infants. The former is easily obtained by a review of an easily read anatomy textbook, such as that by Hollinshead,[1] and the latter by observation of infants and familiarity with the developmental scale of Gesell and Amatruda.[2]

Palpation

Palpation is usually the first step in examining muscles. This can provide information about tenderness and consistency of the muscle bellies. My routine includes palpation of the calf, posterior thigh, biceps, and forearm muscles. Firm, steady, slowly increasing pressure is applied over the thickest part of the muscle.

Generally, a crying infant will change the character of his cry when painful muscles are squeezed. In an older infant or young child the facial expression serves as a good indicator of muscle tenderness. If there is a probability of patient cooperation and one suspects considerable tenderness, this part of the examination should be postponed.

The resistance or "feel" of the muscle when it is palpated can often provide diagnostic information. A normal muscle belly feels firm. This is quite different from the ropy character of partially denervated muscle, the rubbery feeling of a pseudohypertrophic calf, the smooth lack of resistance of a flaccid or hypotonic muscle, the "woodeny" character of a muscle in polymyositis, or the hard, leathery nature of a muscle which has undergone fibrosis.

Making muscle palpation a part of every patient's examination will soon give the examiner confidence in detecting and differentiating muscle abnormalities.

Examination for Muscle Tightness

Muscle tightness often can direct attention to possible muscle weakness. It usually occurs in the muscle group opposite or antagonistic to the weak or paralyzed group. This is because the functioning muscle tends to be held in a shortened position. For example, in a radial nerve injury with paralysis of the wrist and finger extensors, the wrist and finger flexors may be tight. When this muscle is shortened or tight, wrist flexion must occur to provide the necessary slack to fully extend the fingers. In newborn infants with spina bifida and with questionable function in the lower extremities, tightness in a muscle group suggests function in that group.

There are many causes of joint limitation of motion other than muscle tightness, so it is incorrect to suggest that reduced joint motion per se is associated with muscle weakness. Some other causes are bony incongruity, joint effusion, capsular tightness, ligamentous abnormality, and cartilage injury. However, since most muscles cross more than one joint, muscle tightness can usually be recognized as the offender if joint motion is limited for this reason. For example, the hamstring muscle group crosses the hip and the knee, extending the former and flexing the latter. If the hamstrings are tight, that is, shortened, it will be painful and difficult to extend the knee if the hip is flexed. When the hip is extended, the knee may also be extended.

My routine is to check the calf and foot dorsiflexor tightness by dorsiflexing and plantar flexing the ankle respectively. Next, the hamstring group is examined with straight leg raising to 90 degrees with the patient in the supine position. The anterior thigh group is checked by attempting to put the heel to buttocks with the child in the prone position. Back tightness is demonstrated by attempting to put the forehead on the knees, with the patient's legs hanging over the edge of the bed. Most normal children can accomplish these flexibility tests easily. An exception to this generalization is the neonatal infant, who retains hip and knee tightness for four to six weeks after birth.[3]

The upper extremities are examined for muscle tightness in three areas. The shoulder adductors are tested by placing the arm over the head, the elbow extensors and flexors by flexing and extending the elbow, respectively, and the wrist and finger flexors by extending the wrist and finger simultaneously.

Testing Muscle Weakness

In order to understand why certain maneuvers are used to evaluate muscle weakness in infants, it is first necessary to review briefly conventional muscle grading.

In muscle testing several grades are used to indicate the degree of weakness. One common system is as follows: normal, moves through full range against considerable resistance; good, moves through full range against resistance; fair, moves through full range against gravity only; poor, moves through full range with gravity removed (i. e., weight of the part is supported); trace, tendon moves but no joint motion; and, lastly, zero, no function visible or palpable.

Corresponding systems are 100%, 75, 50, 25, 10, 0; 5,4,3,2,1,0; and 0,1,2,3,4,5. The latter two are exactly opposite, one grading strength in reducing order and the other grading weakness in increasing severity. The system used at this hospital is the percentage grade. It has the disadvantage of implying accuracy. However, the first mentioned has the disadvantage of use of adjectives which are commonly used in describing physical findings without a specific meaning. Use of the letters N, G, F, P, Tr, and O removes this objection. The other two grading systems are confusing, since they are exactly opposite.

In all of the above methods there are two, admittedly arbitrary, but convenient reference points: first, zero or no function and, second, enough function to move the part against gravity. For example, the grade for the function of the quadriceps if it extends the knee can be said to be fair, 50%, or 3. Function in this muscle can also be said to be "antigravity" or "gravity plus." Conventionally, this

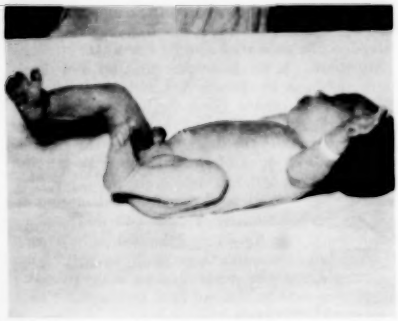


Fig. 1.—Moro embrace reflex. Note that lower extremities participate also.

middle grade is used only with the proximal limb muscles and the trunk muscles, since the distal groups move such small and therefore light parts of the body. In the distal groups of the extremity, function is noted and can be grossly estimated by the tension of the appropriate tendon.

Cooperation is always relative. In infants and small children the child developmentalist can, with time and persistence, usually elicit a desired activity. However, in a busy physician's office, it is more practical to consider this age group as relatively uncooperative and proceed with maneuvers to obtain desired muscle function in the shortest possible time.

When testing muscle groups in children below the age of cooperation, usually 3 or 4 years, it is most useful to divide them into two categories: those who cannot walk and those who can walk. The former includes infants who have not yet reached that stage of motor development and those older children who by reason of disease or injury cannot walk.

The reason for this division is that walking gives considerable information about muscle function in the lower extremities, the trunk, and, surprisingly enough, the upper extremities. Also, walking can be generally stimulated regardless of cooperation. Byers [4] suggested that often muscle abnormalities were first noted when the child began to walk. This is a common occurrence in my experience. Therefore, in infants and small children who cannot walk it is necessary to elicit muscle function in other ways.

Examination of the Infant

Two steps are apparent in order to examine muscle groups of infants. First, it is necessary to position the infant so that the muscle group being tested can lift the appropriate part of the body against gravity, and, second, the muscle group must be made to contract. This latter step may be difficult. Sometimes the infant will spontaneously move the part desired. In fact, some of the textbooks [5] suggest that many diagnoses of motor weakness can be made by an experienced pediatrician's observation of an infant's activity. Most of the waking time of newborn infants is spent in constant activity. Relative weakness of an extremity may be detected by observing reduced activity. In the older infant the time factor often precludes this approach, since desired function probably will not appear spontaneously.

During the first quarter of the first year of life, most of the activity is reflex in nature. Therefore, it is usually necessary to use reflexes to elicit the desired muscle function in the infant up to 3 or 4 months of age. I routinely examine for the following reflexes [6]:

First, the tonic neck reflex is present at birth and disappears at about 4 months of age. When the head is turned to the side, the arm and leg extend on that side and the arm and leg flex on the opposite side. This is used to elicit knee and elbow flexion and extension.

Second, the grasp reflex is present at birth and disappears at about 4 months of age. The infant's fingers will tighten around an object placed in them. This can demonstrate finger flexion weakness, as in Klumpke's paralysis.

Third, Landau's reflex appears from 6 to 12 months of age and disappears at about 3 years. When the infant is held in the prone position, the head, trunk, and legs extend. This is useful in detecting weakness of the hip extensors and the neck and trunk extensors.

Fourth, the Moro embrace reflex [7] is present at birth and disappears by 4 months of age (fig. 1). When the table on each side of a supine infant is struck with the hands, the infant's arms are thrown

out in an embrace attitude describing an arc and tending to approach one another with a tremor. Fingers at first extend and then clench. Similar, though less marked movements, occur with the lower extremities. It becomes asymmetrical when there is weakness of one extremity, as in birth injury with laceration of peripheral nerve (Erb's palsy).

The character of the deep tendon reflexes is occasionally helpful in directing attention to muscle weakness; however, the responses are variable in newborn infants because of the motor activity.[8] The order of their appearance after birth is also variable.

Voluntary motor activity in the infant appears in a cephalocaudal manner. It is useful to simplify the motor development of the first year of life by quarters. In the first three months the infant controls his eyes, in the second three months his head and arms, in the third three months his trunk and hands, and in the last three months his legs, feet, and thumb opposition. Familiarity with developmental patterns is necessary for two reasons. First, voluntary motor activity is used in assessing muscle weakness, and, second, delay in motor development may represent the first sign of weakness.

When activity is present, either spontaneous or elicited, relative weakness of an extremity can be discovered by either of two maneuvers. The one I use most commonly is that of superimposing rapid alternating passive movements on the spontaneous

Fig. 2.—Superimposing rapid passive alternating motions on infant's lower extremities. Resistance to such motion is noted in determination of muscle weakness.

activity, for example, extending and flexing the legs alternately (fig. 2). The weak extremity will resist this movement with less force. Another method is to restrain the spontaneous activity of an extremity and note the force tending to continue the motion.

If the motor activity is not present spontaneously and has not been elicited by the techniques thus far mentioned, then noxious stimuli are used. For example, pinching an extremity with the infant supine or prone, depending on the group to be tested, will usually result in a withdrawal movement which will demonstrate function in the appropriate muscle group. When one desires to test function in the

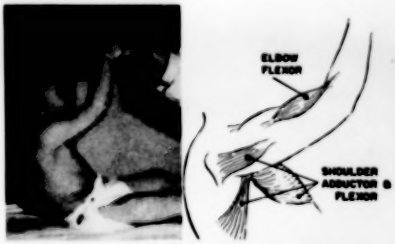


Fig. 3.—Knop test, showing supine infant being pulled to sitting position.

triceps and deltoid, it is useful to position the forearm and hand so that it will drop on the face. This will usually cause extension at the shoulder and the elbow and can easily demonstrate weakness in these groups. Often, placing a corner of the sheet over the infant's face will result in function of the upper extremities, either reflex or voluntary, to attempt removal.

Stroking the sole of the forefoot will cause dorsiflexion of the foot; stroking the heel will cause plantar flexion. With the infant in the prone position and the lower extremities hanging over the edge of the examining table, stroking of the posterior thigh and buttocks will cause the hip to extend, as well as the knee to flex.

I also make the Knop test[9] (fig. 3) a regular part of the examination of each infant. With the infant supine, the hands are grasped and the baby is pulled to the sitting position. The degree of head lag and the attitude of the shoulders and the elbows give clues about arm and neck weakness. Next, the feet are grasped and the buttocks lifted off the table to elicit hip and knee weakness. Although Knop used this to describe the newborn infant's dynamics, it is useful in older infants and children and has been a part of the neurological examination for many years. If there is a head lag after the infant is 4 or 5 months of age, it is suggestive of weakness of the neck flexors or other pathological states resulting in hypotonia of this muscle group. If there is muscle weakness of one leg or arm, that extremity will straighten while the normal extremity will flex at the knee and hip when the lower extremities are lifted.

The shoulder adductors and the scapular stabilizers can also be tested by lifting the infant or child under the armpits with the fingers extended. When

these groups are weak or hypotonic, the patient will slide through the examiner's hands. To make this test more sensitive, the infant is gently tossed in the air a few inches and caught in this position.

Chaney and McGraw [9] found that almost one-third of newborn infants would bear weight on the lower extremities when held in the erect position. A

Fig. 4.—Infant held erect to demonstrate reciprocal motions of legs. Infant shown was 4 days old.

similar proportion demonstrated crawling motions when held in the prone position. Perlstein and Barnett [10] noted that reciprocal motions of the lower extremities are present by 2 to 3 months of age at the latest when the infant is held in the erect position (fig. 4). These motor activities can often guide the examiner to discovery of muscle weakness of the lower extremities. Thus, in the space of a few moments, the infant can be pulled to a sitting position, held in erect position, tossed and caught under the armpits, and suspended in the prone position for a fair estimation of the general muscle strength. When the examiner's attention is directed to a possible area of weakness, specific muscle function can be elicited.

Observing spontaneous activity, eliciting reflex activity, understanding normal motor development, and using ingenuity to stimulate specific groups provide a systematic approach to detecting muscle weakness in children under one year of age.

Examination of the Walking Child

Active walking is associated with considerable muscle activity, so that muscle weakness in the trunk and lower extremities can be discerned. Although the gait pattern is not stabilized until about the age of 7, the requirements of maintaining an erect posture over two moving extremities are such that careful analysis of the child's gait pattern will provide clues about muscle weakness. If the gait appears relatively normal, the child can be made to walk on his toes and on his heels and then run and hop, squat, and stand up to bring out less apparent difficulties. The child of 2 years can run after a fashion and at 3 years runs well, but he usually cannot hop until 4½ years of age.

The walking base of the small child is often mentioned during the neurological examination. This is the distance between the medial edge of the heels when they are in the same frontal plane. Such descriptions as wide and narrow are applied to the base without really specific values in mind. There are factors which alter the width of the base other than neurological factors, for example, the angle between tibia and femur and the femoral neck angle. Generally, a wide base, more than 3 or 4 in. if there is no genu valgum, points to genuine instability in a child who has walked for four to six months.

Fig. 5.—Standing on toes to demonstrate function of gastroc-soleus group.

If the child is taken from his parents and set on the floor 10 or 15 ft. away, he will usually rise to the standing position, run to his parent, there rise on his toes, and reach with his arms outstretched. This provides a good estimation of the strength of the proximal groups of the lower extremities as he

stands and of the proximal groups of the upper extremities and the gastrocnemius-soleus groups when he reaches his parents. If the parent is not present, the same result can be easily accomplished by taking the child away from his bed (fig. 5).

If it is impossible to get the child to walk on his heels, the foot groups are tested by stroking the sole of his forefoot, or, in the standing position, if the patient is distracted in the opposite direction of the pull of the muscle group to be tested, the muscle will contract in an attempt to regain balance. This is done with a finger over the tendon, which immediately tenses as the appropriate muscle contracts. Groups which can be tested with this technique are the "guy wire" muscles of the feet, that is, posterior tibial, anterior tibial, peroneal, and gastrocnemius-soleus.

Holding the child with the examiner's arm around the upper thighs and allowing the patient to jackknife forward and then extend his head and trunk will give a good estimate of the neck, back, and hip extensors (fig. 6). This, in effect, is using the Landau reflex.

Abdominal muscles are best tested by sit-ups. It has been recognized for some time that a child cannot come to the sitting position when lying supine without using hands until the age of 4 or 5. In my experience, 4 years has been the average age. I believe that this is related to the migration of the center of gravity of the body, which at about the age of 3 passes caudal to the umbilicus.[11] This means that until this age more than 50% of the body weight is above the axis around which the trunk flexors act, putting them at considerable disadvantage. To insure maximum effort in the sit-up test it is helpful to assist the child by pulling on a few strands of hair as he attempts to come to the sitting position.

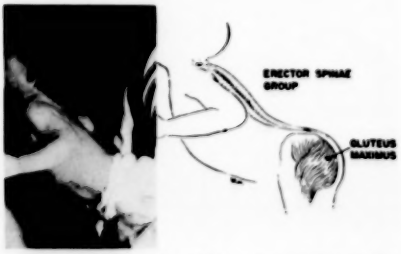


Fig. 6.—Holding child by thighs to demonstrate trunk and hip extensor function.

In the cooperative child, it has been a constant observation that, when instructed to hold the part against the examiner's resistance, if there is true muscle weakness present he will assist with an uninvolved extremity, either hand or leg.

As the examination is concluded, dressing techniques are used to elicit muscle function previously unobtained or to verify earlier observations. The relieved young child will often cooperate quite well in raising his arms to put on a blouse, shirt, or coat held rather high (fig. 7). This can demonstrate anti-

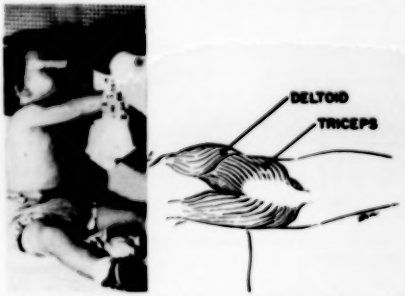


Fig. 7.—Dressing technique to demonstrate triceps and deltoid function.

gravity function of the proximal upper extremity muscles. He will often bear his weight well on one leg as his pants are put on and raise his leg and foot for socks and shoes.

No mention has been made thus far about the importance of the history. On several occasions during the past year I have been asked to see small children who, their parents insist, fall frequently or behave abnormally in terms of motor development. Although I have been unable to demonstrate clinical weakness, I always believe the parent and go to the laboratory for objective assistance in detecting disease of the motor unit.

Electromyographic Examination

The most sensitive method to date of detecting abnormalities of the motor unit is the electromyographic examination. The electromyograph is composed of an electrode system, an amplifier, an oscilloscope, a loud-speaker, and a storing device, such as a camera or tape recorder (fig. 8). It picks up, amplifies, and indicates the action potential of the muscle fiber. This is the electrical activity immediately preceding the contraction.

A group of muscle fibers numbering from a few to 1,000 or more, depending on the muscle, together with the lower motor neuron is termed the motor unit. The summation of the action potentials of the muscle fibers comprising the motor unit is viewed on the oscilloscope and heard over the loud-speaker as a motor unit action potential. Disease or injury of the motor unit alters the pattern of voltages picked up by the electromyograph.

Diagnostic potentials in the various clinical conditions affecting the motor unit are present when the muscle is at rest, as well as when the muscle is active. Thus, a similar situation to the clinical examination exists in the electromyographic examination. First, the voltages must be noted when the muscle is at rest, at both insertional and spontaneous activity, and then when it is active, at both minimal and maximal contraction. Techniques to obtain specific muscle group activity have been described, but it is a most difficult problem to obtain muscle relaxation in an infant or small child. This is especially difficult in a newborn infant in the waking state. This also presents a problem when the child is in the uncooperative age, that is, between 1 and 3½ or 4 years of age, when the child is easily frightened and upset in a strange environment. The procedure itself is associated with a minor amount of discomfort; however, the semidarkened room and the noises over the loud-speaker often serve to disturb the small child even more. In general, the most satisfactory examinations are done in children under 1 and over 4 years of age. In the latter age group they are usually old enough to understand and follow instructions. In preparing the child for the examination, it is suggested to them that they "will see their muscles on television." A simultaneous pinch or slap with insertion of the needle electrode will usually allow the insertion to pass unnoticed. The presence of a parent in the room during the examination is absolutely interdicted.

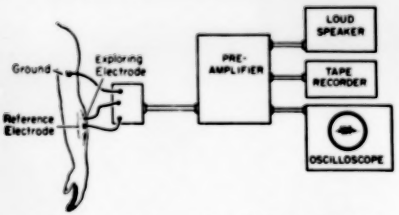


Fig. 8.—Schematic representation of components of electromyograph.

The approach I use to the electromyographic examination in an infant or an uncooperative small child is to examine first muscles which are inactive, usually, for example, the intrinsic muscles of the hands and feet, that is, extensor digitorum brevis, abductor digiti quinti pedis, opponens, hypothenar eminence, and first dorsal interosseus. The opponens is generally not active voluntarily until the child is 36 to 38 weeks of age.

Second, the muscle to be examined is positioned in a most unfavorable position for activity. This is usually, but not always, in its shortest length. In examination of the anterior tibial, dorsiflexion of the foot to an extreme degree will often discourage muscle contraction (fig. 9). Conversely, the long head of the triceps is usually not active with the elbow flexed to more than 120 degrees.

As was mentioned previously, most of the difficulty is with children from the ages of 1 to 4 years. Here it is felt that sedation is occasionally helpful; however, if used too heavily, one is unable to obtain maximum contraction, and, if it is used in smaller dosages, the child will become aroused after one or two muscles have been investigated. During the past year, with an average of 50 electromyographic examinations each month, of which at least half were in children, it has been found necessary to use sedation in only two instances. Once an electromyographic abnormality is demonstrated, the next problem is to determine the distribution of that abnormality. This requires investigation of muscles other than those mentioned earlier, so that the examiner's patience and ingenuity is tested.

An additional determination which adds another dimension to electromyography is the measurement of the nerve conduction velocity. This is helpful in localizing diseases of the motor unit to the axon of the lower motor neuron. It is the stimulation of the motor nerve at two locations along its course, photographing the stimulus artifact and the muscle response with an appropriate time base. After the distance on the skin between two points of stimulation is measured, counting the time base between stimulus artifact and the muscle response on the photograph, the nerve conduction velocity is calculated in meters per second. This is usually reduced in chronic diseases affecting the axon, such as infectious neuronitis, regenerating injured peripheral nerves, and polyneuritides of various types. The nerves most accessible for this study are the ulnar and median nerves in the forearm and the common

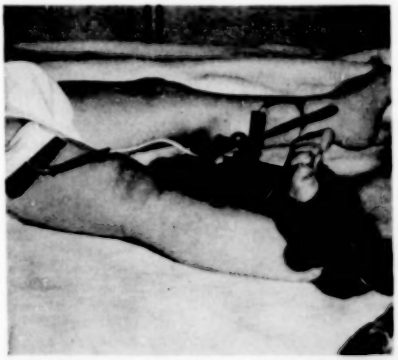


Fig. 9.—Foot in passive dorsiflexion to discourage voluntary activity of anterior tibial. Note position of needle electrode and ground.

peroneal nerve and posterior tibial in the leg. In these nerves the conduction velocity varies from 45-70 meters per second in the adult. The conduction velocity of newborn infants is reduced [12] and does not approach the adult standards until the child is 3 or 4 years of age.

The accurate clinical determination of muscle weakness in an infant or uncooperative small child is of paramount importance in the proper diagnosis of diseases of the motor unit. If the history or examination suggests weakness which cannot be localized clinically, the electromyographic examination can prove very helpful. The following case illustrates this point.

A 3-year-old boy was admitted to Children's Hospital in November, 1957, with a chief complaint of "not walking right." For several months he had been complaining of stiffness and soreness of his muscles without a clear-cut febrile illness. Physicians, including a neurologist, pediatrician, orthopedist, and internist, had entertained diagnoses from poliomyelitis to no disease present. Physical examination demonstrated mild generalized symmetrical weakness with function of the proximal limb muscles rated as barely "antigravity." Palpation of muscle bellies suggested increased resistance and elicited moderate tenderness. The electromyogram showed small, short, duration potentials with increased proportion of polyphasic potentials and many fibrillation potentials. This was interpreted as most suggestive of polymyositis. The serum transaminase level was within the upper limits of normal. Muscle biopsy showed degenerative muscle fibers with round cell infiltration. When reexamined in six months, he had developed characteristic skin lesions of dermatomyositis.

Summary

The detection of muscle weakness in infants and small children depends on three principles: (1) understanding the normal motor developmental pattern of infants, (2) knowing functional anatomy, and (3) developing techniques to elicit specific muscle group activity.

Using these three approaches, any physician dealing with this age group can become surprisingly adept in the diagnosis of muscle weakness. When the clinical examination suggests weakness or the physician suspects a disease or injury of the motor unit in the absence of physical findings, the most sensitive method of detecting and localizing such pathology used to date is the electromyographic examination.

Children's Hospital, 17th Street at Livingston Park.

References

1. Hollinshead, W. H.: Functional Anatomy of the Limbs and Back, Philadelphia, W. B. Saunders Company, 1951.

2. Gesell, A., and Amatruda, C. S.: Developmental Diagnosis, ed. 2, New York, Paul B. Hoeber, Inc., 1947.

3. Zausmer, E.: Evaluation of Strength and Motor Development in Infants: II, Phys. Therapy Rev. **33**:621-629 (Dec.) 1953.

4. Byers, R. K.: Evolution of Hemiplegias in Infancy, Am. J. Dis. Child. **61**:915-927 (May) 1941.

5. Green, M., and Richmond, J. B.: Pediatric Diagnosis, Philadelphia, W. B. Saunders Company, 1954. Sachs, B., and Hausman, L.: Nervous and Mental Diseases from Birth Through Adolescence, New York, Paul B. Hoeber, Inc., 1926. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1944.

6. Chaney, L. B., and McGraw, M. B.: Reflexes and Other Motor Activities in Newborn Infants: Report of 125 Cases as Preliminary Study of Infant Behavior, Bull. Neurol. Inst. New York **2**:1-56 (March) 1932.

7. Gordon, M. B.: Moro Embrace Reflex in Infancy: Its Incidence and Significance, Am. J. Dis. Child. **38**:26-34 (July) 1929.

8. Burr, C. W.: Reflexes in Early Infancy, Am. J. Dis. Child. **21**:529-533 (June) 1921.

9. Knop, C.: Dynamics of Newly Born Babies, J. Pediat. **29**:721-728 (Dec.) 1946.

10. Perlstein, M. A., and Barnett, H. E.: Nature and Recognition of Cerebral Palsy in Infancy, J. A. M. A. **148**:1389-1397 (April 19) 1952.

11. Palmer, C. E.: Studies of Center of Gravity in Human Body, Child Development **15**:99-180 (June-Sept.) 1944.

12. Lambert, E. H.: Personal communication to the author.

STRESS AND DIABETES.—On clinical, statistical and experimental evidence all forms of stress play an important part in the disturbance of good control in diabetes. The effect of emotional stress, usually anxiety, is apparent in the older group of mild, obese, insulin-resistant cases. In the younger group of acute, thin, insulin-sensitive diabetics, stress due to associated endocrine imbalance is more common. It is probable that emotional stress is never the sole etiological agent in diabetes, but may have an additive or precipitating effect. As no single diabetogenic hormone has yet been isolated it is assumed that the mechanism is under hypothalamic control and may be in the nature of an overflow from adrenocorticotropic, gonadotropic and thyrotropic hormones stimulating the growth hormone. . . . Attention is drawn to the association of the premenstrual syndrome, stress, and fluctuation in diabetic control. Recurrent coma seems to occur in individuals of poor moral stamina and inadequate personality who, on one pretext or another, omit their insulin and lapse into coma to avoid an unpleasant life situation. A plea is made for the management of certain categories of diabetics in special units where the staff can become interested and competent to care for them in such a way as to give maximum security, education and encouragement.—J. B. Walker, M.D., Stress and Diabetes, *The Practitioner*, May, 1957.

TREATMENT OF THROMBOSIS WITH FIBRINOLYSIN (PLASMIN)

Joseph E. Sokal, M.D., Julian L. Ambrus, M.D., Ph.D.
and
Clara M. Ambrus, M.D., Ph.D., Buffalo

The possibility of dissolving a recent thrombus by the intravenous administration of a fibrinolytic enzyme was studied in a series of patients. Fibrinolysin (plasmin) was prepared in several ways from human and bovine plasma, and preparations were obtained from other laboratories also. Altogether 114 infusions of fibrinolysin were given to 37 volunteer patients, most of whom had incurable cancer. Thirteen episodes of acute thrombophlebitis, occurring in 10 patients of this series, were treated. In five of the eight cases in which the age of the thrombus was three days or less, complete resolution was obtained. When improvement did occur, the pattern of response was fairly uniform; pain was relieved within 24 hours, color improved and tenderness disappeared shortly thereafter, and edema disappeared within a few days. The results, which were sometimes striking, are illustrated in 14 case histories. Fibrinolysin was ineffective when given a week or more after the first manifestations of thrombosis, and it did not prevent the formation of fresh thrombi. The mechanism of its action upon blood clots in vitro as well as the clinical experiences here reported argue in favor of simultaneous administration of anticoagulants with fibrinolysin in the management of acute thromboses.

Arterial and venous thromboses are a major cause of morbidity and mortality. Much has been accomplished in recent years to lessen the toll of thrombotic diseases through the use of anticoagulant therapy, often continued for years or for life, in patients who have had serious thrombotic episodes. However, anticoagulant therapy serves only to prevent further thrombotic complications; it does not remove clots which have already formed. Several attempts have been made to treat acute thromboses with agents that showed promise of dissolving existing thrombi. Potent proteolytic enzymes, such as trypsin and chymotrypsin, have been administered locally or systemically to patients suffering from vascular thromboses or from diseases characterized by undesirable fibrin deposition.[1] Although the local administration of such enzymes is widely practiced, systemic use has not met with general acceptance. In addition to such hazards as sensitization to foreign protein and the severe side-reactions which may follow systemic administration in adequate doses, the lack of specificity of these enzymes is a serious disadvantage. Studies in this laboratory indicated that systemic doses of trypsin, chymotrypsin, crude pancreatic protease, papain, and ficin, sufficient to produce intravascular lysis of experimental clots in dogs, also produced falls in the levels of several proteins involved in the blood clotting system, occasionally resulting in fatal hemorrhage.[2] Only preparations of fibrinolysin (plasmin) were able to lyse venous or arterial clots at nontoxic concentrations.

Fibrinolysin is a proteolytic enzyme which manifests selective affinity for fibrin as a substrate.[3] Its physiological role is believed to be the lysis of the fibrin deposits in blood vessels and tissues which result from the minor injuries and spontaneous thromboses of everyday life.[3c] Many excellent reviews dealing with fibrinolysin have appeared in recent years.[4] The following account is a somewhat simplified summary of our present knowledge of this important biological agent.

Fibrinolysin absorbs selectively to fibrin and hydrolyzes it into smaller soluble fragments. Free fibrinolysin is not normally found in the blood. A precursor, profibrinolysin (plasminogen) is a normal constituent of the plasma. Profibrinolysin is transformed to fibrinolysin by a number of activators found in tissues and in various secretions (urine, tears, milk, saliva, and seminal fluid). In the latter areas, profibrinolysin activators may play a physiological role in keeping narrow channels of excretion open. Tissue activators may appear in the circulation during stress, muscular exercise, and hypoxia and after epinephrine injections. Blood also contains an antifibrinolysin factor which can rapidly neutralize fibrinolysin.

The physiological relationship of clotting mechanisms to the fibrinolytic system is illustrated in figure 1. When tissues are damaged, thromboplastin is liberated and the complex mechanism of clotting, leading to fibrin deposition, is initiated. Fibrin promotes hemostasis and forms a matrix for reparative processes. Profibrinolysin (plasminogen) activators are also released at the injured site. Circulating profibrinolysin is locally converted into fibrinolysin, binds to the fibrin fibers, and dissolves

From the Roswell Park Memorial Institute and the University of Buffalo Medical School.

them after a period of time. Thus, repair can proceed without scar formation. Circulating antifibrinolysin binds and inactivates any excess of free fibrinolysin in the circulation.

In some disease states, notably, carcinoma of the prostate, large amounts of free fibrinolysin appear in the blood and lead to a hemorrhagic diathesis. On the other hand, we have seen some patients who suffered from repeated thromboses and were found to have very high levels of circulating antifibrinolysin. Deficiencies in the fibrinolytic system were recently implicated in the development of atherosclerotic lesions on the basis of excessive fibrin deposits in the intima.[26]

We have investigated various methods of preparation and purification of fibrinolysin, starting with crude profibrinolysin fractions obtained from pooled human or bovine plasma. Changes in preparative technique have resulted in major alterations in the fibrinolytic activity of the final product. In some cases we encountered considerable variation in potency from batch to batch, even when the same technique of preparation was used. In general, however, we have been able to produce fibrinolysin of satisfactory potency by several different methods. A number of preparations were obtained from other investigators. A large number of different preparations were tested in animals for in vivo fibrinolytic

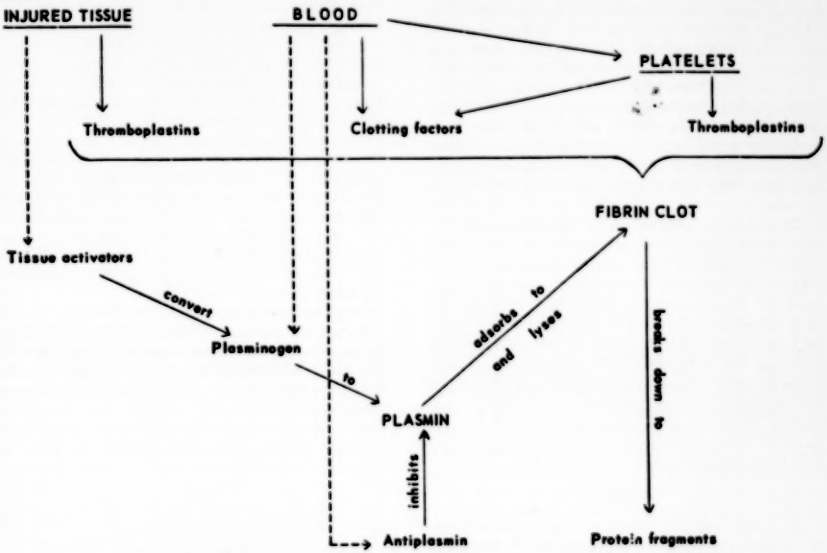


Fig. 1.—Simplified diagram of relationship between blood clotting and fibrinolytic systems.

Human profibrinolysin is obtained as a product of blood plasma fractionation. It can be activated artificially in several ways. A potent activator is bacterial streptokinase. Almost as potent is the enzyme urokinase, derived from human urine. Spontaneous conversion of profibrinolysin to fibrinolysin takes place under certain physical and chemical conditions; however, this is an inefficient way to prepare fibrinolysin. Bovine fibrinolysin can be produced by activation with chloroform. The physical and biochemical properties of fibrinolysin vary somewhat with different methods of activation and preparation.[5]

activity. These studies have been reported in detail.[26] A brief summary follows: Radioactive arterial and venous clots were produced in dogs, rabbits, and monkeys. Semiconstricting ligatures were left in place to prevent dislodgment of the clots. The fate of the clots was followed in several ways—by continuous recording of radioactivity over vessel segments containing the clots, by phlebography with iodopyracet (Diodrast), and, in some cases, by direct visualization. Control clots remained in place satisfactorily and showed only slight declines in radioactivity over periods of seven days. Although the vessels remained effectively obstructed, small amounts of iodopyracet were seen to pass the

thrombosed segments, indicating that the fibrin meshwork did not completely block blood flow and that intravenously administered agents may be able to permeate the interstices of a fresh clot. Serial histological studies of clots induced in dogs showed beginning endothelialization and organization of clots at three days, proceeding rapidly thereafter.[6] Fibrinolysin was infused intravenously at a distant site at various time intervals after the formation of radioactive clots in dogs. When the interval between formation of the clot and administration of fibrinolysin was 72 hours or less, clot lysis was observed in most experiments. This was demonstrated by decrease or disappearance of radioactivity over the vessel segment, by phlebographic visualization of open vascular segments, and, in superficial clots, by direct observation. Clots three days of age or older showed only partial or no lysis.[7] Acute and subacute pharmacological studies in mice, guinea pigs, rabbits, dogs, and monkeys were performed with various potent preparations of fibrinolysin. With most preparations no significant toxic manifestations were observed at dosage levels considerably in excess of those required to produce in vivo clot lysis. Most preparations were nonpyrogenic for rabbits.

On the basis of these animal experiments, several fibrinolysin preparations were selected for trial in man. The patients used were volunteers, most of whom had incurable cancer. The principal indications for therapy were acute and subacute peripheral thromboses and certain edematous states. Since one of the principal purposes of this study was to compare the side-effects of various preparations, patients were accepted for treatment even though the diagnosis was questionable. Such cases are excluded from the therapeutic evaluation, however. In most cases, two or more different preparations were administered during a course of therapy.

Methods

Diagnosis and Evaluation of Therapeutic Effect.—Standard criteria for the diagnosis of thrombophlebitis were used. Most patients gave typical clinical histories of pain and swelling of an extremity developing rapidly over a period of a few hours to two days. A few bedridden patients were observed to have developed edema and cyanosis of a leg overnight without spontaneous pain. In cases of superficial thrombophlebitis, typical signs of inflammatory reaction over the involved veins were observed. In such cases, thrombosed veins could be palpated easily. All patients had tenderness over the involved area. Homans' sign was positive in patients with deep thrombophlebitis of the calf. Lowenberg's cuff test[8] was used as a quantitative measure of compression tenderness. In a few cases, venous occlusion was demonstrated by contrast venography. The age of the thrombophlebitis was estimated from the clinical history. Onset was dated from the first definite symptoms or signs.

Serial observations of the following points were carried out on all patients diagnosed as having thrombophlebitis: evaluation of symptoms, presence of Homans' sign, results of Lowenberg's cuff test, circumference of extremity at several points, degree of edema, intensity of cyanosis, and degree of visible inflammatory reaction. A typical clinical progress sheet is discussed below. In some cases, skin temperature recordings were obtained at several points. Evaluation of therapeutic response was based on these observations. In one case, reopening of major venous channels was demonstrated by venography. No patient is listed as having a "complete resolution" unless the signs and symptoms of thrombophlebitis disappeared within one week of the beginning of therapy. Patients were classified as "improved" if marked resolution by most criteria occurred within one week but some abnormalities persisted.

Arterial occlusion was diagnosed by the typical history of rapidly developing pain, coldness and discoloration in an extremity associated with the characteristic findings of pallor or mottling, and absent arterial pulses below the point of occlusion. The diagnosis was confirmed by determination of skin oxygen tension before and after inhalation of pure oxygen.[9] The application of this method is illustrated below.

Other diagnoses were made by the usual clinical criteria and require no detailed discussion here. In all cases, patients were examined by two or more physicians not associated with this project and the diagnoses under which patients are classified were unanimously agreed on.

Additional Clinical and Laboratory Observations.—Before, during, and after fibrinolysin infusions determinations were obtained of blood pressure, pulse rate, respiration rate, temperature, electrocardiographic tracing, basal metabolic rate, hemoglobin level, hematocrit value, white blood cell, platelet, and differential counts, blood fibrinolysin, profibrinolysin, and antifibrinolysin levels,[10] fibrinogen level, prothrombin time, and Lee-White coagulation time. In some cases more detailed study of factors of the blood clotting system was undertaken.

Fibrinolysin Preparations.—The fibrinolysin preparations used in this study were of five general types, as follows: (*a*) human profibrinolysin prepared from pooled plasma obtained from the American Red Cross Blood Program, activated with an excess of crude streptokinase (Varidase or Streptokinase); (*b*) various purified fractions of the above, from which much material of streptococcic origin had been removed; (*c*) human profibrinolysin activated with human urokinase; (*d*) human profibrinolysin allowed to activate spontaneously; and (*e*) bovine profibrinolysin activated with

chloroform. Details of the methods of preparation of these fractions and their individual characteristics will be presented elsewhere.[10]

Fibrinolysin was administered by intravenous infusion over a two-to-four-hour period. The usual dose was 15 Loomis units [11] per kilogram of body weight, administered in 500 to 1,000 ml. of saline solution. All preparations of fibrinolysin were found to lose activity rapidly at room temperature. Infusion bottles were therefore placed in a refrigerated holder.

Results

A total of 114 infusions of fibrinolysin was given to 37 patients. Side-reactions to these infusions varied greatly, depending on the preparation used. There was also moderate variation among different patients receiving the same preparation.

The worst side-reactions were induced by preparations containing an excess of crude streptokinase. Malaise, nausea, tachycardia, and cutaneous vasoconstriction were the initial manifestations of these reactions and appeared about one to two hours after the beginning of the infusion. Elevation of the basal metabolic rate was noted at this time. Soon afterward, one or more shaking chills occurred, followed by fever. The basal metabolic rate rose as much as 150%. Premedication with antipyretics, analgesics, chlorpromazine, and antihistamines reduced the intensity of these reactions but did not abolish them. Intravenously given amobarbital sodium (sodium Amytal) or thiopental (Pentothal) sodium, administered during the premonitory stage of malaise in doses sufficient to induce sleep, completely prevented the chills and reversed the cutaneous vasoconstriction. This medication was effective in arresting chills even when given during the height of these reactions. However, the elevation of metabolic rate and the height of the temperature were not affected by these hypnotics, even though muscular contractions and heat conservation by the skin were blocked. Increase in blood pressure was noted during the early stages of these severe reactions and was sometimes followed by hypotensive episodes two to six hours after the infusion. In a few patients, electrocardiographic changes were observed during the height of the reaction. Recovery from these side-reactions was complete within 2 to 12 hours.

Variation of the methods of preparation and of the activators used resulted in a series of preparations with decreased toxicity. Finally, two human fibrinolysin preparations were obtained which produced slight or no side-effects. One of these was a purified, streptokinase-activated preparation; the other was activated with urokinase. Even the nontoxic streptokinase-activated preparations were antigenic and resulted in the production of antistreptokinase antibodies and skin sensitivity to crude streptokinase. The urokinase-activated preparation did not induce antibody production or skin sensitivity.

Spontaneously activated human fibrinolysin and chloroform-activated bovine fibrinolysin caused few or no side-reactions. However, these preparations appeared to be less effective than the streptokinase-activated or urokinase-activated human preparations.

The therapeutic results in 26 episodes suitable for evaluation are discussed below.

Peripheral Thrombophlebitis.—Thirteen episodes of acute thrombophlebitis, occurring in 10 patients, were treated. In addition to fibrinolysin therapy, standard nursing procedures and conservative symptomatic therapy were employed, including bed rest, a cradle to lift bed covers over the affected extremities, analgesics, sedatives, and other treatments. In seven instances, anticoagulant therapy was withheld until fibrinolysin treatment and evaluation of the response was completed. Antibiotics were administered in one case. The age of the thrombotic processes at the time of institution of therapy was one day or less in six instances, 2 to 3 days in two instances, 4 to 5 days in four instances, and 10 days in one.

Table 1 presents the therapeutic response in these cases. Complete resolution was obtained in five of the eight instances where the age of the process was three days or less, and definite improvement was seen in one other. Among the older processes, complete resolution was seen in one, improvement in two, and no effect in two. The pattern of response was relatively uniform in the cases where improvement was observed. Pain was relieved rapidly and usually disappeared within the first 24 hours. Color changes and tenderness to pressure were the next to respond. Resolution of edema took longer and was sometimes incomplete several days after all other signs had disappeared. Since most of these patients had disseminated intra-abdominal cancer, however, it is difficult to evaluate the significance of the slow clearing of edema. Partial obstruction of pelvic and abdominal veins and lymphatics may have been the principal reason for the slow response in many of these cases. Individual case reports follow:

Case 1.—A 34-year-old woman with far-advanced carcinoma of the stomach and intreperitoneal dissemination developed acute thrombophlebitis of the left leg. The leg was obviously swollen and cyanotic; distended superficial veins could be seen. Homans' sign and the cuff compression test were strongly positive. Fibrinolysin therapy was started about 24 hours after onset of thrombophlebitis. She had moderately severe side-reactions to the first infusion, with malaise, chills, temperature of 103.2 F (39.5 C), and basal metabolic rate of +117%, in spite of premedication with 0.6 Gm. of aminopyrine and 50 mg. of chlorpromazine. On the following morning the color of the left leg was almost normal. Homans' sign was equivocal, and there was subjective improvement. The second infusion induced a mild febrile reaction, with a maximum temperature of 101 F

(38.3 C). Rapid improvement continued. Homans' sign became negative on the third morning, and treatment was discontinued. There was still slight edema of the leg at this time. Two days later, however, the leg appeared entirely normal and there were no signs or symptoms of thrombophlebitis. Table 2 presents some of the clinical observations recorded during therapy and is illustrative of the techniques used to evaluate results in this series. The patient's general condition deteriorated rapidly, and she died a few days later. Shortly before death, signs of venous thrombosis again appeared. Autopsy revealed a fresh thrombus in the left iliac vein and pulmonary embolization.

asymptomatic and ambulatory, Homans' sign was negative, and the leg appeared normal. Anticoagulants were not administered, and the patient was discharged a week later.

Two days after discharge, the patient returned with acute thrombophlebitis of the deep veins of the left leg, of about one day's duration. The leg was edematous and highly sensitive to pressure. Homans' sign was strongly positive. Venograms were obtained by applying a tourniquet above the ankle and forcibly injecting diatrizoate (Hypaque) sodium into a superficial vein of the dorsal surface of the foot. The dye dissipated slowly and filled only the superficial veins of the leg. All deep venous channels appeared to be oc-

Table 1.—*Clinical Course of Ten Patients with Thrombophlebitis Treated with Fibrinolysin*

Case, No.	Involvement	Age of Process, Days	No. of Fibrinolysin Infusions/Days	Other Therapy	Response, No. of Days After First Fibrinolysin Infusion: Pain-Free Motion	Color Normal	No Edema	Homans' Sign Negative	Serial Phlebograms
1	Deep, left leg	1	4/2	...	1	1	4	2	
2	Deep, right leg	4-5	6/6	...	1	2	6	4	
	Deep, left leg	1	7/6	...	1	2	Incomplete effect	3	Opening of thrombosed veins
3	Superficial, left leg	10	6/6	...	No effect				
	Superficial, right forearm	1	4/4	Heparin	Transient partial improvement				
	Superficial, left shoulder	1	3/3	Heparin	1	2	2		
4	Deep, left calf	1	5/5	Heparin, bishydroxycoumarin	No effect				Progression of thrombosis
5	Deep, right calf	1	4/4	Heparin, bishydroxycoumarin	1	1	4	2	
6	Superficial and deep, right leg	2	2/1	...	1	2	2	1	
7	Deep, left leg	3	4/3	...	2	2	2	3	
8	Deep, right leg	4-5	2/2	Heparin	1	6	6		No change
9	Deep, left leg and femoral artery	5	4/3	Heparin	4	4	Incomplete effect	3	
10	Deep, right leg	5	1/1	...	No effect				

Table 2.—*Criteria of Response to Fibrinolysin Therapy in Case 1**

Date and Treatment	Color of Leg	Cuff Test, Mm. Hg† Arm Right	Arm Left	Thigh Right	Thigh Left	Calf Right	Calf Left	Homans' Sign	Circumference, Cm. Thigh Right	Thigh Left	Calf Right	Calf Left	Subjective Report on Left Leg
1/16.....	Mottled	200	180	100	90	100	80	+	38	44	30.5	35.5	Heavy, warm
1/17 Fibrinolysin, 5 units/kg. of body weight.....	Less mottled	170	180	80	80	110	70	+	38	44	30	35	Heavy
5 units/kg. of body weight.....	Only trace mottling	200	200	120	80	100	80	+	38	44	30	34	Heavy
1/18 Fibrinolysin, 5 units/kg. of body weight.....	Almost normal	220	200	110	80	90	100	±	35.5	38.5	29	35.5	Heavy, feels better
10 units/kg. of body weight													
1/19.....	Normal	150	240	150	120	140	105	−	35	38	31	36	Not different from other leg
1/21.....	Normal	200	180	130	130	150	140	−	37	38	30	33	Normal

* Inoperable gastric carcinoma, gastric hemorrhage, and thrombophlebitis of left leg.
† End-point, report of pain by patient.

Case 2.—A 39-year-old woman with advanced metastatic ovarian adenocarcinoma developed thrombophlebitis of the deep veins of the right leg. The process was four to five days old when she was referred to us. The leg was obviously swollen. Homans' sign and Loweuberg's cuff test were positive. Temperature was 100.6 F (38 C). Fibrinolysin was administered daily for five days. The first infusion induced mild chills, lasting about 10 minutes. There were no side-reactions to subsequent treatment. Sixteen hours after the first infusion, the patient reported that the right leg became "less tight" and she could bend it for the first time in several days. There was a slight decrease in the pressure sensitivity of the right calf. On the following day there was further decrease in pressure sensitivity and in the circumference of the right leg. Rapid improvement continued. On the fourth day, pressure sensitivities in the two legs were equal and Homans' sign was equivocal. After one week, the patient was cluded (fig. 2*A*). Fibrinolysin was administered for six days, with mild reactions on two occasions. Pain subsided within 24 hours, and she was able to move the leg without difficulty. Pressure sensitivity returned to normal in two days. Homans' sign became negative after three days. The circumference of the leg decreased but did not return to the prethrombosis level. Repeat venograms, with identical technique, demonstrated reopening of the tibial vein (fig. 2*B*). The patient was then treated with heparin and bishydroxycoumarin and was discharged a week later on maintenance bishydroxycoumarin therapy. Two months after discharge the patient was doing well, without recurrence of thrombosis.

Case 3.—A 72-year-old woman with agnogenic myeloid metaplasia and a history of several hemorrhagic and thrombophlebitic episodes was admitted with pain and swelling of the left leg of about 10 days' duration. Pitting edema of the leg and marked inflammatory reaction along the course of

the superficial saphenous vein were noted. The thrombosed vein was palpable and exquisitely tender. Platelet count was 2,500,000 per cubic millimeter. Venography revealed occlusion of the major superficial veins, but patent deep veins. Fibrinolysin was administered for four days with one moderately severe reaction and one mild reaction. No improvement was seen; pain persisted and edema of the extremity increased. Heparin therapy was instituted, but it proved difficult to hold the clotting time within therapeutic limits; the patient appeared to require much more than the usual doses of heparin. During the following days additional areas of thrombophlebitis appeared, involving the right forearm and the left upper arm and shoulder (sites of intravenous therapy). Fibrinolysin therapy was reinstituted, and the dosage of heparin was increased. Only partial and transient improvement was noted in the superficial thrombophlebitis of the right forearm. However, the edema, tenderness, and inflammatory reaction of the left upper arm, shoulder, and anterior part of the chest resolved completely in 48 hours. Edema of the left leg and thigh increased. Fibrinolysin therapy was discontinued, but energetic anticoagulant therapy was maintained. Slow, gradual improvement in the areas of residual thrombosis occurred during the next two months.

Case 4.—A 74-year-old man with inoperable adenocarcinoma of the rectum underwent sigmoid colostomy. Nine days later he developed pain and swelling of the left calf. Homans' sign and Lowenberg's cuff test were equivocal. Venograms showed thrombosis of the posterior tibial vein and partial obstruction of the anterior tibial and femoral veins. Fibrinolysin therapy was started on the following day and continued for five days. He also received anticoagulant therapy with heparin and bishydroxycoumarin. He had a mild reaction to the third fibrinolysin infusion and a moderately severe reaction, followed by a hypotensive episode, after the fifth infusion. The leg remained swollen. Repeat venograms one week after the initial study showed progression of the thrombotic process, with extension of the femoral thrombosis. Gradual improvement in the condition of the leg occurred during the next four weeks, but some edema was still present at the time of discharge.

Case 5.—A 62-year-old man with generalized arteriosclerosis, arteriosclerotic heart disease, and carcinoma of the urethra underwent radical curative surgery and had a prolonged convalescence. One month after the operation he complained of pain in the right leg. On examination the leg was found to be warm and swollen. Homans' sign and Lowenberg's cuff test were positive. Heparin and bishydroxycoumarin were administered, and fibrinolysin therapy was started. He received four infusions of fibrinolysin on successive days, with mild reactions to the first three. Striking subjective improvement and decrease in edema were noted on the morning after the first infusion. One day later, Homans' sign became negative. Four days after the first fibrinolysin infusion, the leg was entirely normal.

Case 6.—A 74-year-old woman with carcinoma of the cervix, arteriosclerotic heart disease, and a history of bilateral thrombophlebitis of the legs and prophylactic femoral vein ligations done five years previously developed pain in the right calf. On examination one day later, she had a strongly positive Homans' sign and an inflamed, tender area on the medial aspect of the calf. She was considered to have both superficial and deep thrombophlebitis. She received two infusions of fibrinolysin, with moderately severe chills and fever after the second dose. On the morning after the first infusion, Homans' sign was negative and the area of superficial involvement was strikingly improved. By the following day, there were no residue of the acute episode.

Case 7.—A 52-year-old woman was intermittently treated with radiation for 10 years in another hospital for lymphosarcoma. During the follow-up observation period, she developed adenocarcinoma of the cervix. Intravaginal radium treatment was given. After completion of therapy, tenderness and swelling of the left leg appeared. Homans' sign and Lowenberg's cuff test were positive. Fibrinolysin therapy was started about 40 hours after the first sign of thrombophlebitis and was continued for three days. A moderately severe pyrogenic reaction followed the first infusion; there were no side-effects during the subsequent treatments. Homans' sign became equivocal, pressure sensitivity decreased, and there was marked reduction of edema on the day after the first fibrinolysin infusion. Rapid improvement continued, and resolution was essentially complete on the third day. The patient was then given heparin for several weeks. Six months after discontinuation of heparin and discharge, she was active without any complaints.

Case 8.—A 68-year-old woman underwent resection of a carcinoma of the bladder. Nine days later, she noted swelling and slight pain in the right foot. Four days after the onset

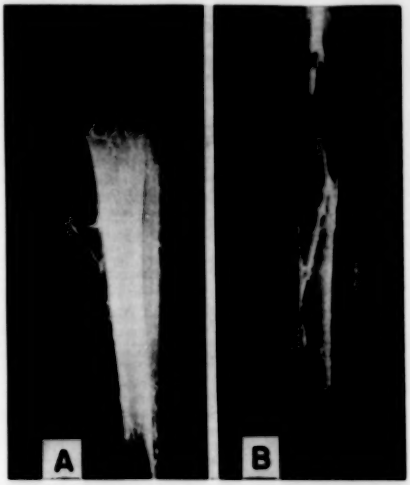


Fig. 2. (case 2).—Venograms of left leg taken, *A*, immediately before and, *B*, six days after beginning of fibrinolysin therapy. Previously occluded deep venous channels are now patent.

of the process, she had 2+ edema of the right leg below the knee and dilated superficial veins of the leg. Homans' sign was negative; Lowenberg's cuff test was weakly positive. Venogram revealed obstruction of the posterior tibial vein. She received two infusions of fibrinolysin, on the fifth and sixth days after the swelling was discovered. She was also treated with heparin and bishydroxycoumarin. Repeat venogram on the seventh day showed no change. However, she improved rapidly, and the extremity was entirely normal three days later.

Case 9.—A 73-year-old woman with agnogenic myeloid metaplasia was admitted with swelling and pain of the left leg, of about five days' duration, and coldness and pain of the left foot, of one day's duration. The entire left extremity was swollen and tender. The foot was pale and cold; the leg exhibited bluish mottling; skin temperature was increased above the knee; and there was erythema and tenderness over

the femoral vein. The left femoral pulse was diminished as compared to the right. The left popliteal and dorsalis pedis pulses were absent. The clinical impression was (1) left femoral thrombophlebitis and (2) arterial occlusion above the knee, due to either thrombosis or intense vasospasm. The patient was given heparin, and fibrinolysin therapy was instituted. She received four infusions of fibrinolysin during the 72 hours after admission, with mild to moderately severe reactions. Penicillin was also administered. On the morning after the first infusion, signs of arterial obstruction were no longer present but evidence of femoral thrombophlebitis and major venous obstruction persisted. Three days later, she was strikingly improved, but some edema of the leg was still present. More gradual improvement continued, bishydroxycoumarin was substituted for heparin therapy, and she was discharged one month later.

Case 10.—A 59-year-old woman had carcinoma of the ovary, with abdominal carcinomatosis, ascites, and moderate edema of both legs. Six hours after abdominal paracentesis, her right leg became painful, cyanotic, and more edematous. On succeeding days, the edema progressed to involve the entire extremity. Five days after the onset of thrombosis, the extremity was still painful, cyanotic, and markedly edematous. Homans' sign and Lowenberg's cuff test were strongly positive. She was given one infusion of fibrinolysin, with a moderately severe reaction. There was no improvement. Her general condition continued to deteriorate rapidly, and she died two days later. Autopsy revealed a thrombus completely occluding the right femoral vein.

Arterial Thrombosis and Embolism.—Arterial blood flow was restored eight hours after the administration of fibrinolysin in a case of probable popliteal artery thrombosis (case 9). A case of arterial embolism in a patient with advanced vascular disease was treated one day after the acute episode and embolectomy, without success. No favorable response was observed in another patient; the summary of this case follows.

Case 11.—A 53-year-old man with metastatic renal carcinoma, who also suffered from intermittent claudication of three years' duration, developed a series of superficial venous thromboses and an episode of pulmonary embolism and infarction. Anticoagulant therapy was administered. Hepatomegaly was present, with nodular hepatic masses. Needle biopsy of the liver was planned, and for this reason heparin therapy was discontinued. Two days later, pain, cyanosis, and ecchymoses developed in the left foot. Femoral pulse was present, but the popliteal, posterior tibial, and dorsalis pedis pulses could not be felt. Skin temperatures and oxygen tensions were lower than in symmetrical contralateral points. Breathing of pure oxygen resulted in increase of skin oxygen tension in the right leg and in the left thigh, but no changes occurred at points below the left knee. Table 3 presents some of the observations recorded in this patient and is illustrative of the procedures we are now using in suspected arterial occlusion. Fibrinolysin therapy was started about 24 hours after the first clinical signs were observed and was continued for two days. The patient was given heparin. A moderately severe pyrogenic reaction followed the second fibrinolysin infusion. No improvement was noticed, and eventually dry gangrene of the left foot and thrombophlebitis of the deep veins of the right leg developed, in spite of continued heparin therapy. The patient died two weeks later in hepatic coma. Autopsy revealed organized thrombi in the left popliteal artery and right popliteal vein.

Other Indications.—Several cases of edema, presumably secondary to venous or lymphatic obstruction, were treated. Two are of particular interest.

Case 12.—A 60-year-old man with carcinoma of the right tonsil, previously treated with radiation, developed acute swelling of the left side of the head and neck (fig. 3A). Palpebral edema prevented opening of the eyelids, and the patient complained of headache. The etiology of this episode was uncertain, but thrombosis of major veins draining this area was suspected. He was given two infusions of fibrinolysin on successive days, with mild side-effects. Penicillin therapy was also initiated, but cultures taken before treatment were later reported to be sterile. Five hours after the first infusion, there was a marked reduction in swelling of the face and the patient could open his eyelids. On the following morning, the head and neck appeared normal except for some redness of the face and slight edema of the mastoid area. During the next two days there was a complete return to normal status (fig. 3*B*).

Case 13.—A 43-year-old woman with recurrent postoperative bilateral adenocarcinoma of the breast was treated with androgens, oophorectomy, radiation, and hypophysectomy. She developed edema of the right shoulder and arm, presumably related to tumor extension. Later, marked edema of the hand appeared (fig. 4A). She was comatose, and no subjective information could be obtained. Fibrinolysin therapy was given about three days after the appearance of edema of the hand. Moderate chills and fever developed. Ten hours later, definite reduction of swelling was observed. There was slight oozing from the lesions of the chest wall, starting during the infusion and gradually subsiding. By the following morning, the edema of the right hand and forearm had completely disappeared (fig. 4*B*). No further treatment was given. During the next three days the edema gradually recurred.

Table 3.—*Diagnostic Criteria in Case 11**

Date and Treatment	Color of Left Leg	Arterial Pulses, Left Leg: Femoral	Popliteal	Anterior Tibial	Dorsalis Pedis	Skin Temperature at Reference Points,† Degrees Centigrade: Left Leg A	Left Leg C	Left Leg F	Right Leg A	Right Leg C	Right Leg F	Relative Available Oxygen Tension of Skin Before and After Breathing 100% Oxygen: Left Leg A Air	Left Leg A Oxygen	Left Leg C Air	Left Leg C Oxygen	Left Leg G Air	Left Leg G Oxygen	Right Leg C Air	Right Leg C Oxygen
2/21 15 units/kg. of body weight	Cyanosis, ecchymosis	+	—	—	—	28.0	29.0	32.0	30.0	31.8	32.1	16	17	17	22	30	52	170	279
2/22 30 units/kg. of body weight	Increased cyanosis	+	—	—	—	28.0	29.9	31.1	31.4	32.0	31.1								
2/23	Livid	+	—	—	—	27.0	28.8	32.0	30.0	32.0	32.3	17	17	28	28	40	42	60	76
2/24	Livid	+	—	—	—	26.9	30.0	32.0	29.5	30.0	32.1								

* Metastatic renal carcinoma, severe peripheral vascular disease, and thrombosis of left popliteal artery.
† A = dorsum of foot, C = mid-calf, F = mid-thigh, G = patella.

Five patients with chronic edema of an extremity, of 3 to 12 months' duration, did not respond to fibrinolysin therapy. Three of these were women with postmastectomy edema of the arm. Two were women with intrapelvic cancer and edema of a lower extremity.

Three instances of skin flap cyanosis, in two patients, were treated. It was postulated that this disorder might be secondary to multiple thrombosis

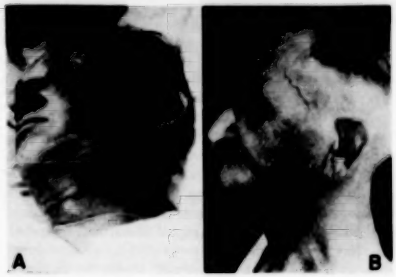


Fig. 3 (case 12).—*A*, before and, *B*, two days after beginning of fibrinolysin therapy. Edema has disappeared.

of small vessels in the flap. One patient, treated eight days after the onset of cyanosis, did not respond. The other, treated promptly on each of two occasions, showed rapid improvement both times.

Case 14.—A 59-year-old man had a large basal cell carcinoma of the right side of the back. A pedicle flap was formed to repair the skin defect to be produced by surgical therapy. A month later a second delay dorsal flap was formed. Cyanosis of the flap developed, possibly due to small thrombi. Fibrinolysin therapy was instituted 24 hours after this occurrence and maintained for five days. Mild pyrogenic reactions were observed on the second and fifth days. There was definite improvement in the color of the flap after one day of treatment, and it was normal on the fifth day. Five days later slight cyanosis was again noticed. Fibrinolysin was administered for two days, without side-effects. By the third day the color of the flap was again normal. Three weeks later, the tumor was excised and skin grafting accomplished. The patient was discharged in good health two months later.

Comment

We have administered a relatively large number of different preparations of fibrinolysin to a relatively small number of patients, with the objective of identifying preparations suitable for clinical use in acutely and seriously ill patients. In most cases, several preparations were given to the same patient in order to compare side-effects more accurately. Several of the preparations we have tested appear satisfactory for general use. Detailed data on the methods of preparation, pharmacology, and clinical, biochemical, and hematological effects of these fibrinolysin preparations will be presented elsewhere.[10]

Our results suggest that fresh thromboses can be beneficially affected by fibrinolysin therapy. Of eight episodes of thrombophlebitis of three days' duration or less, complete resolution within one week was obtained in five and marked improvement in one. The natural history of this disease is quite variable, and our series of treated cases is small. It would be unwise to draw sweeping conclusions from this limited experience. However, the results in these patients parallel our observations in experimental animals and suggest that fibrinolysin may prove to be a useful therapeutic agent in this common and distressing disease. It is improbable that the majority of such seriously ill patients as ours would have had spontaneous resolution of their thrombotic processes in less than a week. In two cases of classic thrombophlebitis (cases 1 and 2) and one case of probable thrombosis complicating infiltrating carcinoma (case 13), the clinical syndrome recurred soon after termination of fibrinolysin therapy. The improvement associated with fibrinolysin therapy cannot, therefore, be ascribed to a coincidental remission of the tendency toward thrombosis in these patients. The venograms shown in figure 2 demonstrate that reopening of thrombosed channels actually occurred. To achieve this by the normal processes of organization and recanalization would require weeks or months.

The rapid subsidence of edema in the patients in cases 12 and 13 was quite striking. We believe that these cases represent silent venous thrombosis, with successful clot lysis by fibrinolysin. They were not included among the cases of thrombophlebitis, however, because of the lack of satisfactory criteria, other than edema, for making such a diagnosis. Similarly, in case 14, it appears reasonable to assume that the skin flap cyanosis was due to multiple small thromboses and that the improvement reflected lysis of these thrombi. However, proof

Fig. 4 (case 13).—*A*, before and, *B*, one day after single infusion of fibrinolysin. Edema of right hand and lower forearm has disappeared.

of this hypothesis would have required biopsy of the flap, a procedure not considered desirable by the attending surgeon.

In our experience, fibrinolysin has proved useful only in acute thromboses. However, Cliffton [12] reported beneficial results in certain instances of thrombosis of relatively long standing.

Anticoagulants were deliberately withheld in many of our patients in order to make the test of fibrinolysin therapy as severe as possible. Since these patients had terminal cancer, we felt this was justifiable. However, fibrinolysin does not prevent the development of new thrombi, as demonstrated by the patient in case 3, who developed additional thromboses while undergoing fibrinolysin therapy. We believe, therefore, that the ideal management of acute thromboses should include anticoagulant therapy. In future cases, we plan to administer heparin immediately after the first fibrinolysin infusion and to maintain anticoagulant therapy for the usual period after clinical resolution.

Our experience in this series has impressed us with the difficulties of exact diagnosis of peripheral thrombosis and of evaluation of therapeutic responses. It is well known that thrombosis may be entirely silent. Many of the classic diagnostic criteria of venous thrombosis depend on the presence of an associated inflammatory response. If the inflammatory signs appear late, the age of the thrombotic process may be considerably underestimated. This may perhaps explain our therapeutic failure in a patient such as in case 4, who seemed to have an ideal case and who was treated "early" and aggressively with fibrinolysin and anticoagulants. On the other hand, subsidence of inflammation and restoration of normal circulation through an efficient collateral system can simulate complete reversal of the thrombotic process, when in fact there has been no dissolution of the clot. This was the situation in the patient in case 8, who would have been listed as having a "complete resolution," had not venograms been obtained before and after treatment. In patients with disseminated abdominal and pelvic tumors, such as in case 2, edema of a leg may persist even though the major venous channel has been reopened. Because of these difficulties, we have turned increasingly toward the use of serial venograms in our cases of thrombophlebitis. This technique improves the accuracy of diagnosis and makes the evaluation of therapeutic response much more precise.

Comparable difficulties were encountered in the evaluation of early arterial thrombosis. Coldness of an extremity may be due simply to cutaneous vasoconstriction. Palpation of arterial pulses at the knee and ankle is often difficult, even in patients who do not have arterial obstruction. These difficulties can be surmounted by the use of complex techniques, such as those employed in case 11. Failure of low tissue oxygen tensions to rise during inhalation of pure oxygen demonstrates unequivocally that arterial perfusion of the extremity has been interrupted. Even this technique, however, cannot differentiate between acute thrombosis, embolism, and intense arterial spasm causing almost total reduction of blood flow. In many cases, the exact diagnosis is made retrospectively. Thus, in case 11, a failure, the diagnosis of arterial thrombosis was proved by the development of gangrene and by the autopsy findings. However, in the patient in case 9, with a similar clinical picture and recovery, it cannot be stated with absolute certainty that arterial thrombosis was present. Somewhat similar findings have been reported in cases of acute massive thrombophlebitis.[13] However, the fact that signs of arterial obstruction followed the onset of thrombophlebitis by four days in our patient suggests that this was, in fact, a separate event.

We have not treated patients with coronary thrombosis in this study because we did not wish to submit such seriously ill patients to the possible hazards of side-reactions to fibrinolysin infusion and to the dangers of withholding anticoagulant therapy. However, the most important uses of fibrinolysin may well prove to be in treatment of acute coronary and cerebral thrombosis, where the natural consequences of the thrombotic process are so much more serious than in peripheral thrombophlebitis. A major purpose of the study reported here has been to develop preparations of fibrinolysin which can be administered safely to patients with acute coronary thrombosis. We now have several such preparations and hope to initiate a controlled clinical study of fibrinolysin therapy in coronary and cerebral thrombosis in the near future.

Sherry and Alkjaersig,[9a] Johnson and associates,[14] and Miller [15] demonstrated therapeutic effects in inflammatory and thrombotic conditions with intravenous, intramuscular, and buccal administration of streptokinase only. Presumably, these effects resulted from activation of patients' own profibrinolysin. If therapeutic levels of active fibrinolysin can be obtained consistently by such techniques, they may prove to be simpler methods of therapy than the administration of preformed fibrinolysin. The fact that streptokinase is a very potent antigen and may induce severe sensitivity reactions in man [10] may be a disadvantage of this approach, however.

Summary

Various preparations of the fibrinolytic enzyme, fibrinolysin (plasmin), have been administered to patients with thrombotic disorders. Rapid resolution of signs and symptoms has been observed in patients treated within a few days of the apparent clinical onset of thrombosis. Fibrinolysin therapy was ineffective when started one week or more after the first manifestations of thrombosis.

Many of the fibrinolysin preparations tested were deemed unsatisfactory because of low potency or a high incidence of side-reactions or because they were strongly antigenic and carried the hazard of inducing sensitization to streptococcic products. However, several preparations appear satisfactory for futher clinical trial in acute peripheral thromboses and in coronary and cerebral thrombosis.

Several patients treated only with fibrinolysin suffered recurrence of thrombosis soon after the completion of therapy. We believe, therefore, that fibrinolysin treatment should be supplemented by anticoagulant therapy to prevent such recurrent thromboses.

It must be emphasized that this approach to the therapy of acute thrombosis is still experimental. Much more work needs to be done before fibrinolysin can be recommended for general use.

666 Elm St. (3) (Dr. Sokal).

Chester Kucinski (University of Buffalo) and Arthur Eisen (University of Pennsylvania) participated in these studies as summer fellows. L. Alicandro, R.N., and A. Higgins, R.N. (research nurses), D. Reddington, B.S., I. Mink, B.S., and R. Shields, B.S. (technicians) provided technical assistance in these studies.

Several preparations of profibrinolysin and streptokinase-activated fibrinolysin used in this study were supplied by Drs. D. L. Kline and S. B. Fishman of Yale University, and K. H. Bayer, G. Bayne, and W. Baumgarten of Merck Sharp & Dohme, division of Merck & Co., Inc., Philadelphia. The chloroform-activated fibrinolysin used in this study was supplied by Drs. A. C. Bratton, M. F. Fahey, E. C. Loomis, and E. Weston of Parke, Davis & Company, Detroit. One of the urokinase preparations used in this study was supplied by J. Ploug of Leo Pharm. Co., Copenhagen, Denmark. Fraction 3 of human plasma used in this study was provided by Dr. J. N. Ashwort of the American Red Cross Blood Program, through E. R. Squibb and Sons, New York.

This study was supported, in part, by grants from the American Heart Association; the National Institutes of Health, U. S. Public Health Service; Merck Sharp & Dohme, division of Merck & Co., Inc.; and Parke, Davis & Company.

References

1. Innerfield, I.: Trypsin Given Intramuscularly in Chronic, Recurrent Thrombophlebitis, J. A. M. A. **156**:1056-1058 (Nov. 13) 1954. Taylor, A.; Overman, R. S.; and Wright, I. S.: Studies with Crystalline Trypsin: Results and Hazards of Intravenous Administration and Its Postulated Role in Blood Coagulation, ibid. **155**:347-351 (May 22) 1954.

2. (*a*) Ambrus, J. L.; Back, N.; Mihalyi, E.; and Ambrus, C. M.: Quantitative Method for in Vivo Testing of Fibrinolytic Agents: Effect of Intravenous Trypsin on Radioactive Thrombi and Emboli, Circulation Res. **4**:430-439 (July) 1956. (*b*) Ambrus, J. L., and others: Clinical and Experimental Studies on Fibrinolytic Enzymes, Ann. New York Acad. Sc. **68**:97-137 (Aug.) 1957.

3. (*a*) Sherry, S., and Alkjaersig, N.: Biochemical, Experimental, and Clinical Studies of Proteolytic Enzymes: With Particular Reference to Fibrinolytic Enzyme of Human Plasma, Ann. New York Acad. Sc. **68**:52-66 (Aug. 30) 1957. (*b*) Astrup, T.: Fibrinolysis in Organism, Blood **11**:781-806 (Sept.) 1956. (*c*) Astrup, T.: Biological Significance of Fibrinolysis, Lancet **2**:565-568 (Sept. 15) 1956. (*d*) MacFarlane, R. G., and Biggs, R.: Fibrinolysis: Its Mechanism and Significance, Blood **3**:1167-1187 (Oct.) 1948. Reference 2*b*.

4. Reference 3*b*, *c*, and *d*.

5. Markus, G.; Ambrus, C. M.; Whistler, F. C.; and Woernley, D. L.: Studies on Activation of Human Plasminogen, Fed. Proc. **17**:104 (March) 1958.

6. Back, N.; Ambrus, J. L.; Simpson, C. L.; and Shulman, S.: Study on Effect of Streptokinase-Activated Plasmin (Fibrinolysin) on Clots in Various Stages of Organization, J. Clin. Invest. **37**:864-871 (June) 1958.

7. References 6 and 2*b*.

8. Lowenberg, R. I.: Early Diagnosis of Phlebothrombosis with Aid of New Clinical Test, J. A. M. A. **155**:1566-1570 (Aug. 28) 1954.

9. Urbach, F., and Noell, W. K.: Effects of Oxygen Breathing on Tumor Oxygen Measured Polarographically, J. Appl. Physiol. **13**:61-65 (July) 1958.

10. Ambrus, J. L., and others: Comparative Clinical Studies of Various Preparations of Plasmin, to be published.

11. Loomis, E. C.; George, C., Jr.; and Ryder, A.: Fibrinolysin: Nomenclature, Unit, Assay, Preparation and Properties, Arch. Biochem. **12**:1-5 (Jan.) 1947.

12. Cliffton, E. E.: Use of Plasmin in Humans, Ann. New York Acad. Sc. **68**:209-229 (Aug. 30) 1957.

13. Edwards, W. S.: Observations on Pathogenesis and Management of Massive Venous Occlusion, Surgery **43**:153-163 (Jan.) 1958.

14. Johnson, A. J.; Fletcher, A. P.; McCarty, W. R.; and Tillett, W. S.: Effects in Patients of Intravenous Infusions of Purified Streptokinase Preparations, Proc. Soc. Exper. Biol. & Med. **94**:254-258 (Feb.) 1957.

15. Miller, J. M.: Anti-inflammatory Effect of Intramuscular Streptokinase, Ann. New York Acad. Sc. **68**:185-191 (Aug. 30) 1957.

IRON-DEFICIENCY ANEMIA.—Several factors are thought to contribute to the iron-deficiency anemia of infancy. Included among these are decreased dietary iron, inadequate iron stores at birth, and excessively rapid growth. . . . Of the factors investigated the most frequently found was an abnormal diet. In those cases in which only one cause was found the large majority were due to abnormal diet. Low birth weight was much less frequently the single factor, and low maternal iron stores never acted alone, although in a larger series the latter factor might have been implicated as operating singly. Abnormal weight increment in full-term infants was also only rarely encountered as a cause of iron-deficiency anemia. It appears, therefore, that, given a normal diet, an infant overcomes his relative neonatal iron deficit. However, normal iron stores at birth are not adequate to prevent the development of iron-deficiency anemia in the presence of an abnormal diet.—J. P. Dawson, M.D., and J. F. Desforges, M.D., Dietary and Storage Factors in Iron-Deficiency Anemia of Infancy, *A. M. A. Journal of Diseases of Children*, August, 1958.

SPINAL ANESTHESIA FROM THE SURGEON'S STANDPOINT

Robert A. Scarborough, M.D., San Francisco

Spinal anesthesia has certain advantages over other types in operations below the level of the diaphragm. It gives a degree of muscular relaxation that cannot be attained in general anesthesia, even if relaxant drugs are used, without undesirable depression of respiratory and circulatory functions. In the author's experience with 5,000 operations with the use of spinal anesthesia there have been no deaths and no instances of permanent motor paralysis. It is assumed that both surgeon and anesthesiologist are on the alert for such possible complications as nervous apprehension, nausea, vomiting, respiratory depression, and cardiovascular disturbance. Postoperative urinary retention necessitated catheterization in approximately 30% of this series; it is doubtful whether this figure differs significantly from that for colonic and anorectal surgery under general anesthesia. The incidence and severity of headache have become negligible since techniques have been improved by using small-gauge lumbar puncture needles, avoiding multiple punctures of the dura, keeping the patient horizontal for at least 24 hours after operation, and making sure of adequate hydration. Two important contraindications are neurological disease and intestinal obstruction. Spinal anesthesia, properly used, has advantages that are especially appreciated by the surgeon operating for colonic and anorectal disease.

I am a representative surgeon who prefers spinal anesthesia for operations below the level of the diaphragm. More specifically, in my own particular field of surgery for colonic and anorectal disease, I believe that spinal anesthesia is the anesthesia of choice.

For anorectal surgery, complete muscular relaxation of the sphincter ani, levator ani, coccygeus, and gluteus muscles is essential for adequate exposure and satisfactory definitive procedure. It is desirable to have the patient in the prone position. When this position is used, it is important to avoid respiratory and circulatory depression. For fulfillment of these conditions low spinal saddle-block anesthesia is unquestionably the anesthesia of choice.

For abdominal surgery, two fundamental requirements are adequate muscular relaxation of the abdominal wall and a quiet, contracted intestine. Again, spinal anesthesia is unexcelled for producing these two conditions. To attain comparable results with general anesthesia requires a depth of anesthesia which produces both a central and a peripheral depression of respiratory ventilation and of circulation.

With the recent introduction of peripheral muscle relaxants, it is now possible to produce more adequate muscle relaxation with higher levels of anesthesia. Today, a well-administered general anesthesia, combined with judicious use of muscle relaxant drugs, more nearly approaches, but does not fully achieve, the distinctive advantages of spinal anesthesia.

As Dripps and Vandam [1] said, "Spinal anesthesia . . . is relatively free from the criticism of toxicity and the mortality associated with general anesthesia . . . the great hazard of spinal anesthesia in the minds of both physician and patient is the possibility of persistent paralysis after the anesthetic effects should have disappeared." In all truth, such hazard does exist, as demonstrated by a number of reported cases in the medical literature.

In 1950, Kennedy and co-workers [2] published a vindictive attack on spinal anesthesia, with a report of 11 tragic examples of severe neurological complications following spinal anesthesia. It was their opinion that paralysis below the waist is too large a price for the patient to pay in order that the surgeon should have a fine relaxed field of operation. There can be no argument with this opinion, provided that the incidence and severity of such complications are sufficient to outweigh the advantages of this form of anesthesia. There is abundant evidence that this is not the case.

Read in the Symposium and Panel Discussion on Spinal Anesthesia before the Joint Meeting of the Section on Anesthesiology and the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Review of the Literature

In the table is listed the reported experience of seven outstanding authorities, supplemented by an additional 5,000 consecutive private patients operated on by myself with use of spinal anesthesia. These are series of consecutive cases numbering from 2,300 to 12,000 in which specific study of the incidence of neurological complications was carried out. Particularly noteworthy is the excellent report by Dripps and Vandam [1] from the University of

Pennsylvania Hospital. This was a comprehensive prearranged plan of study with long-term follow-up of all patients who received spinal anesthesia over a period of four years. In the opinion of these authors this intensified search for suspicious symptoms in all probability increased the number of symptoms and invited extraneous complaints. As an example, they give this reply received from one patient: "After getting your letter I seem to think I am having after-effects."

In these 65,677 cases, there was not a single instance of permanent motor paralysis. Also recorded in the table are four deaths. The two reported by Jackson and Petsch [3] occurred in 1930, in their early experience with spinal anesthesia. The two reported by Sadove and Levin [4] occurred in patients who were moribund before induction of anesthesia and who died of cardiac arrest. Sadove and Levin believe that possibly these patients should have had only refrigeration anesthesia.

Neurological complications reported by these workers were as follows: Transient paresthesias of the lower extremities, most commonly in the skin area supplied by the lateral femoral cutaneous nerves to the thighs, occurred in 93 patients, or 1 in 700 (0.14%). Transient motor weakness in the lower extremities was reported in seven cases, or 1 in 9,000 (0.01%). Transient abducens nerve palsy occurred in eight patients, or 1 in 8,000 (0.012%). Transient backache and muscle spasm occurred in four patients (0.006%). While these are included as possible neurological complications, probably they were skeletal in origin. Mild transient meningismus also was reported in four cases. There was one reported case of aseptic benign meningitis, with complete recovery.

In one patient neurological signs developed, subsequent to spinal anesthesia, which proved to be due to a meningioma of the spinal cord. Cure was effected by definitive surgery for the meningioma. In one case of persistent paralysis of the left peroneal nerve, preexisting symptoms of such paralysis had been present and this was not considered to be a neurological complication of spinal anesthesia. The majority of these reports contained no data on headache after spinal anesthesia. This will be discussed with other postoperative complications.

Complications During Spinal Anesthesia

Both the anesthesiologist and the surgeon must be cognizant of possible untoward reactions during and after spinal anesthesia, so that they may intelligently employ proper procedures of prevention and treatment for such reactions. Complications during anesthesia can include nervous apprehension, nausea and vomiting, respiratory depression, circulatory depression, and cardiac arrest.

Nervous Apprehension.—The patient's apprehension can be minimized by adequate discussion of the procedure with him in advance by both the surgeon and the anesthesiologist. Appropriate sedation should be used, along with "supplemental vocal anesthesia" by the anesthesiologist during the operation. The latter in no way alludes to the utilization of hypnosis.

Nausea and Vomiting.—When nausea and vomiting occur, they are usually proportional to the degree of nervous apprehension on the part of the patient. This may be controlled promptly by minimal amounts of intravenously given meperidine (Demerol) hydrochloride or thiopental (Pentothal) sodium.

Respiratory Depression.—The degree of respiratory depression present is directly related to the level of anesthesia; this is true particularly in paralysis of the intercostal muscles. It may also be caused by injudicious preoperative sedation. When such depression occurs, artificial respiratory exchange and oxygen must be utilized to prevent anoxia and circulatory collapse.

*Review of Reported Experience with Spinal Anesthesia**

Author	Spinal Anesthesias, No.	Deaths, No.
Stein, J. J., and Tovell, R. M.: Am. J. Surg. 30:282, 1935	10,000	0
Hebert, C. L., and others: J. A. M. A. 142:551-557 (Feb. 25) 1950	5,763	0
Bonica, J. J.: Management of Pain, Philadelphia, Lea & Febiger, 1953	12,000	0
Dripps and Vandam[1]	10,098	0
Grady, R. W., and others: Anesthesiology 15:310, 1954	2,300	0
Jackson and Petsch[3]	10,350	2
Sadove and Levin[4]	10,166	2
Present study	5,000	0
Total	65,677	4

* No instance of permanent motor paralysis was reported by these workers.

Circulatory Depression.—In my experience with saddle-block spinal anesthesia for anorectal surgery, rarely does any significant amount of hypotension occur. The average drop in systolic pressure is less than 10 mm. Hg.

In abdominal operations, with the necessity of a higher level of anesthesia, there may occur a serious drop in blood pressure unless the anesthesiologist takes appropriate control measures. In my experience in working with highly qualified anesthesiologists, blood pressure seldom drops more than 20 mm. Hg and, when it does, rarely stays below that level for as long as five minutes. In every abdominal operation continuous intravenous infusion is maintained for fluid and blood replacement and for any indicated intravenous medication.

Cardiac Arrest.—In the collected series of 65,677 spinal anesthesias there were three reported cases of cardiac arrest, with one recovery. Two of these

three patients were moribund before induction of anesthesia. In my experience, cardiac arrest has not yet occurred.

Complications After Spinal Anesthesia

It is axiomatic that the responsibility of the anesthesiologist and the surgeon for the welfare of the patient does not end when the patient is wheeled from the operating room. Appropriate measures need to be taken for the prevention or treatment of four principal postanesthesia complications: hypotension, nausea and vomiting, urinary retention, and headache.

Hypotension.—Any fall in blood pressure produced by spinal anesthesia may recur as long as the anesthesia is effective, unless appropriate control measures are maintained until the effects of the anesthesia have terminated. It is also noteworthy that any sudden movement of the patient during transfer from operating table to bed or Guerney may initiate a significant drop in blood pressure.

Nausea and Vomiting.—In my experience the incidence of nausea and vomiting as a postoperative complication is no greater with spinal anesthesia than with general anesthesia for comparable surgical procedures.

Urinary Retention.—It is generally believed that the incidence of urinary retention in the immediate postoperative period is greater after spinal anesthesia than after general anesthesia. I have never been convinced that this is so, although I can offer no statistical data to refute this belief. Catheterization has been done in approximately 30% of my patients who have had anorectal surgery under spinal anesthesia. This incidence of the use of catheterization in good part reflects an unwillingness to permit overdistention of the bladder in the immediate postoperative period. In my experience there has been no instance of persistent neurogenic dysfunction of the bladder after spinal anesthesia.

Headache.—The incidence of headache after spinal anesthesia is variously reported in the literature as from 1.5 to more than 30%. It is generally agreed that such headache is directly related to the leakage of cerebrospinal fluid at the site of needle puncture of the dura. By employment of a few simple preventive measures, I have found that the incidence and the severity of headache after spinal anesthesia have become negligible. These procedures include the use of a small-gauge lumbar puncture needle, avoidance of multiple punctures of the dura, horizontal position of the patient for at least 24 hours after operation, and adequate hydration.

With the use of these simple preventive measures, only occasionally has it been found necessary to prescribe any specific treatment for headache after spinal anesthesia. In an occasional instance persistent headache, not promptly relieved by placement in the horizontal position, has occurred in tense individuals who have had prolonged nausea and retching after operation. Adequate hydration by intravenous infusion plus medication with tranquilizers to ameliorate nausea and tension has given prompt relief.

Contraindications

It is advisable to avoid the use of spinal anesthesia in patients with any history or signs of neurological disorder or injury or disease of the spinal column. In many instances this is a precautionary measure, to avoid any possible or presumed aggravation of such disorder.

I do not employ spinal anesthesia for abdominal operations in the presence of intestinal obstruction, because of the danger of precipitating intestinal perforation and because of the possibility of regurgitation and aspiration.

When abdominal surgery is considered imperative in a patient who is comatose or in severe shock, I believe that both spinal and general anesthesia are contraindicated and prefer local procaine infiltration or block anesthesia.

I do not consider preexisting cardiovascular disease a contraindication to the use of spinal anesthesia. My experience supports the published conclusion of Lorhan and Merriam[5] that spinal anesthesia is excellent for elderly and poor-risk patients, including those with advanced cardiac and hypertensive disease.

Conclusions

In every patient the selection of the type of anesthesia to be employed should be determined, first, on the basis of safety for the patient and, second, on the basis of relative advantage to the surgeon. In my experience, such selection has resulted in the use of spinal anesthesia for the great majority of operations for colonic and anorectal disease.

490 Post. St. (2).

References

1. Dripps, R. D., and Vandam, L. D.: Long-Term Follow-up of Patients Who Received 10,098 Spinal Anesthetics, J. A. M. A. **156**:1486-1491 (Dec. 18) 1954.

2. Kennedy, F.; Effron, A. S.; and Perry, G.: Grave Spinal Cord Paralyses Caused by Spinal Anesthesia, Surg. Gynec. & Obst. **91**:385-398 (Oct.) 1950.

3. Jackson, A. S., and Petsch, K.: Spinal Anesthesia: Conclusions Based on Its Use in 10,350 Cases at Jackson Clinic, Madison, Wis., J. Internat. Coll. Surgeons **23**:180-187 (Feb.) 1955.

4. Sadove, M. S., and Levin, M. J.: Neurological Complications of Spinal Anesthesia: Statistical Study of More Than 10,000 Consecutive Cases, Illinois M. J. **105**:169-174 (April) 1955.

5. Lorhan, P. H., and Merriam, W.: Spinal Anesthesia: Analysis of Causes of Death in 716 Cases, Surgery **31**:421-428 (March) 1952.

PHARMACOLOGY OF COMPOUNDS USED TO PRODUCE SPINAL ANESTHESIA

Robert M. Featherstone, Ph.D., San Francisco

The features desirable in a good local anesthetic for spinal use are summarized as follows: (1) depression of sensory nerve function; (2) reversible action, with no damage to nerve tissue; (3) selective action on nerve tissue; (4) low systemic toxicity in concentrations used clinically; (5) no irritation or pain at injection site; (6) rapid onset of action; (7) optimum duration of action; (8) solubility in aqueous solutions at usual pH; (9) stability during sterilization and in solution; and (10) compatibility with vasoconstrictors. The duration of the anesthetic action is a matter of greatest importance in spinal anesthesia. Means of increasing the duration are (1) use of another drug, (2) use of continuous spinal anesthesia, or (3) use of vasoconstrictors. The maximal reflex vasoconstriction in unanesthetized areas occurring as a normal part of spinal anesthesia renders patients especially susceptible to shock and hemorrhage.

The several compounds used to produce the extensive nerve block called spinal anesthesia are all members of a group classed as "local anesthetics." They have many characteristics in common, and they are thought to produce their effects in a common manner. The quantitative differences among them result primarily from the influence of the differing chemical structures on such factors as absorption, penetration of membranes, metabolic reactions, and excretion mechanisms. These individual factors achieve more or less importance as we consider the compounds in the special case of spinal anesthesia. This technique was first used in 1899, but cocaine was the drug employed and a number of deaths resulted.

Characteristics of Local Anesthetics

The figure shows the names and structures of five representative compounds which have been more recently used in this field. These are procaine hydrochloride, tetracaine hydrochloride, piperocaine hydrochloride, dibucaine hydrochloride, and lidocaine hydrochloride. The first three of these compounds are tertiary amino esters of aromatic acids, and the last two are amides rather than esters, with the carbamino group turned around in the lidocaine molecule—a rearrangement which in this case can be utilized to achieve excellent local anesthetic activity without the liability of sensitivity reactions from the ester type of compounds.

The characteristic action shared by these compounds is their ability to block nerve conduction when they are applied locally to nerve tissue in sufficient concentration. They act on any part of the nervous system and on every type of nerve fiber from the motor cortex to the peripheral afferent nerve endings. In the spinal cord, a functional transection is provided. The reversible nature of this action and the complete recovery of nerve function allow the production of discrete local paralysis of sensory and motor nerves.

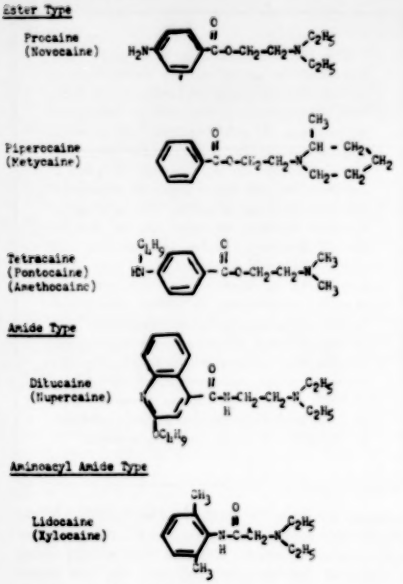
The features desirable in a good local anesthetic for spinal use are summarized as follows: (1) depression of sensory nerve function; (2) reversible action, with no damage to nerve tissue; (3) selective action on nerve tissue; (4) low systemic toxicity in concentrations used clinically; (5) no irritation or pain at injection site; (6) rapid onset of action; (7) optimum duration of action; (8) solubility in aqueous solutions at usual pH; (9) stability during sterilization and in solution; and (10) compatibility with vasoconstrictors. The five compounds being considered are nonirritating and do not injure nerves as they produce anesthesia. In producing spinal anesthesia, such small amounts are used, compared to the amounts used for infiltration, that systemic toxicities are probably not generally a major factor. However, one would choose a compound with the greatest margin of safety if the desirable activity is still equally present, since it is difficult to confine the drug to one spot and the spread may well incapacitate vital processes. The local anesthetics differ from some other groups of compounds, such as barbiturates, in that the anesthetic potencies and toxicities are not strictly proportional. This is perhaps due to the relatively greater nonspecificity of the local anesthetics' action in producing anesthesia and the dependence of their toxicity potentials on specific structural features. Time and lack of detailed knowledge does not permit a much greater exploration of this point.

The duration of the anesthetic action is a matter of greatest importance in spinal anesthesia. The duration is often shorter than is desired. One can increase the time of effect by increasing the dose, but to do this is to invite greater spreading, greater

Professor and Chairman, Department of Pharmacology, University of California School of Medicine at San Francisco.

Read in the Symposium and Panel Discussion on Spinal Anesthesia before the Joint Meeting of the Section on Anesthesiology and the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

absorption, and greater potential toxicity, with an attending greater decrease in blood pressure. Other means of increasing the duration are (1) use of another drug, (2) use of continuous spinal anesthesia, or (3) use of vasoconstrictors. With the continuous technique, the uncertainty of duration can be overcome, the control can be better for high sensory blocks, and a shorter acting drug can be used. Vasoconstrictors work because the anesthetics are not destroyed in the subarachnoid space. Even procaine is not hydrolized. The anesthetic compounds are slowly absorbed systemically and are inactivated. It is thought that they leave the subarachnoid space mostly by venous drainage. Thus, the vasoconstrictors allow up to 100% greater duration of procaine action due to decreased rate of absorption. Epinephrine hydrochloride (0.2 to 0.5 mg.), levarterenol bitartrate (0.5 mg.), and phenylephrine hydrochloride (3 to 10 mg.) have been used. No systemic and no adverse effects on neural tissues are known to occur. The time required for onset of anesthesia would seem to be a relatively minor point for comparison in spinal anesthesia.



Structures of five representative compounds used in spinal anesthesia.

The physical properties of these compounds meet the ideal requirements fairly well, otherwise they would not have been used in this field. They are more soluble in aqueous solvents in acid solutions (lower than pH 7.0) and more soluble in lipids at a slightly alkaline pH; both of these properties are desirable in getting the molecules past an aqueous phase and into a lipid one where they apparently do their work, even though in an extremely local sense they may ionize again within the membrane. If, for some reason, the tissue pH is acid, the free base will not form and the attempt at anesthesia will fail. These relationships are illustrated in the following two equations: (1) $R{:}N{\cdot}HCl + NaHCO_3 \longrightarrow R{:}N + NaCl + H_2CO_3$; (2) $R{:}N + HOH \rightleftharpoons R{:}NH^+ + OH^-$. The most stable compound of the five we are considering seems to be lidocaine, followed by tetracaine, and the other three in a third group. They can all be boiled and autoclaved at 120 C.

It has been noted that the systemic toxicity from these compounds used in spinal anesthesia is generally slight. Nevertheless, there are occasional reports of acute toxic reactions resulting in death from seemingly small amounts of procaine (100 mg.) and tetracaine (10 mg.). Such sensitivity reactions may be eczematous (asthma) or fatal anaphylactic responses; they seem to occur primarily with the procaine or ester type of compound. For want of greater knowledge about mechanisms, not much more can be said about these cases other than the fairly meaningless statements that either they represent an early sigma in the dose-response curve or some special feature of the patient's pathological state has led to the greater sensitivity.

Mechanisms of Action

Pertinent data on these compounds are presented in the table. However, a few other factors deserve brief mention. The volume of solution has a great influence on the level of anesthesia. The area is greater with greater volume. Generally, 1 to 10 ml. is used, depending on the level desired and the extent of control sought through volume. The total amount must be enough to produce nerve block and the desired duration. More drug covers more area and provides longer anesthesia. Operations on the lower part of the abdomen require only a small amount, because little upward diffusion is neces-

Data on Action of Five Local Anesthetics

	Usual Concentrations, %	Volume of Solution, Ml.	Range or Maximum Dose, Mg.	Relative Promptness	Duration, Hr.
Procaine	3.0-5.0	2-5	50-200	2	1-1½
Tetracaine	0.3-0.5	3-5	10-15	2	3-5
Piperocaine	3.0-4.0	3-5	50-200	2	2+
Dibucaine	0.05-0.25	...	3-13	3	4-6*
Lidocaine	2.0-4.0	4	150	1	2½-3

* Suggested by Dr. S. C. Cullen as typical.

sary. As the desired area increases, the total dose must be raised. The degree of increase of dose depends on use of this factor as a control. A slow speed of injection usually allows for a slow diffusion, but increased speed gives greater spread. Barbotage may be used if it is desired to achieve thorough mixing. By changing the composition with such a substance as glucose, the specific gravity can be varied. "Hyperbaric" solutions are those with greater specific gravity than spinal fluid. "Hypobaric" solutions are made by putting drugs in hypotonic solutions. Many anesthetists control the direction of flow both by position of the patient and by the specific gravity.

Let us consider next the mechanism by which these compounds produce anesthesia. I have already stated that these compounds are most stable in their salt forms, that is, in slightly acid solution. However, in the slightly alkaline body fluids, the free base is liberated. This form of the compound is more freely soluble in the lipoid nerve structures and apparently is easily transported to the site where it does its work of depressing sensory nerve perception.

In a physiological sense we can stop there with this explanation of the mechanism, but we would be much more sophisticated if we could say more about this action, as it involves the so-called levels of integration lower than the tissue—the nerve in this case. In other words, what are these compounds doing at the cellular level or at the various subcellular levels—the polymolecular systems, the molecular systems, the molecules, and other systems?

Several so-called theories of action have been proposed, and most of them seem rather incomplete when they are examined critically. The degree of surface tension alteration at oil-water interfaces has been shown to parallel potency. This surface tension change produces decreased permeability of cell membranes, so that there would be a decrease in phasic shifts associated with nerve conduction. Acetylcholine production may be depressed. We have in some way a "stabilization" of the membranes so that the necessary depolarization cannot occur. Pores are closed by the physical presence of these local anesthetic drug molecules. These and other statements have been made to explain the phenomenon. When we look carefully among these phrases, each of which has satisfied some group of experimenters, depending on the limits of their interests, we can still ask the simple questions: "How do the local anesthetics work?" "What are the details of the transmission of the nerve impulse?" Actually, the local anesthetics serve as excellent tools in this important field of research. These compounds do block without depolarizing nerves, therefore are said to "stabilize" conditions in membranes which are normally labile enough to permit phasic shift in potential during impulse conduction. Generally, sensory fibers are blocked first and a separation can be made. There is an order generally to the disappearance of perceptions—pain first, then cold, warmth, touch, and deep pressure, but there is great individual variation. Fiber size seems to be a major determining factor here. Return of blocks to normal occurs in reverse order.

Comment

The chief pharmacological and toxicological effects of local anesthetics are summarized as follows: There is nerve conduction block, and respiration may be depressed. Local anesthetics are central nervous system stimulants; restlessness, tremor, and chronic convulsions may occur. Depression follows with respiratory failure, so that artificial respiration and drug stimulants may be needed. Barbiturates prophylactically are useful. A curare-like action is produced at the myoneural junction. Local anesthetics seem to diminish acetylcholine production.

Cardiovascular actions are as follows: With high systemic concentrations, quinidine-like changes occur in excitability, conduction, and force of contraction. There is arteriolar dilatation. Cardiac arrest may take place either by action on the pacemaker or by sudden onset of ventricular fibrillation, and cardiovascular collapse follows. In regard to circulation, blood pressure may drop in an unpredictable fashion but roughly is proportional to the area of anesthesia. The mechanism of action is disputed: There is paralysis of sympathetic fibers in anterior nerve roots and block of impulses to arterioles and veins; this arteriolar effect leads to a decrease in peripheral resistance and in systolic and diastolic pressures; and the venous effect leads to a postarteriolar pooling of blood, decrease in venous return, and reduced cardiac output. Extreme muscular relaxation of spinal anesthesia contributes to the decreased venous return. Anoxia would further contribute to circulatory inadequacy; final circulatory status depends on balance between these factors.

The maximal reflex vasoconstriction in unanesthetized areas occurring as a normal part of spinal anesthesia renders patients especially susceptible to shock and hemorrhage. Thus, tissues should be handled gently and patients in shock should not have spinal anesthesia.

Fall in blood pressure would be more serious if other drugs did not help. Ephedrine hydrochloride, 50 to 100 mg. intramuscularly, given prior to the spinal anesthestic, may be useful. Other compounds used include phenylephrine, hydroxyamphetamine hydrobromide, and methoxamine hydrochloride.

There is a spasmolytic action on smooth muscles. Also, neurological complications may occur. Apparently, it is difficult to distinguish the role of faulty

technique. The incidence rate is about 1 to 1,000. The most common problem is the cauda equina syndrome. The symptoms are loss of control of sphincters of bladder and intestine and sensory and motor difficulties in the lower extremities. There is slow or no recovery. Less frequent complications are neuritis (radiculitis), myelitis, meningomyelitis, and myeloradiculitis. Many times these are only aggravated and not initiated. Other complications, such as focal cerebral lesions and cerebral nerve palsies, may be secondary to anoxia.

The evaluation of the technique of spinal anesthesia and the relative merits of single dose and continuous procedures are definitely in the sphere of the anesthetists and the surgeons who follow this program.

SPINAL ANESTHESIA, ARACHNOIDITIS, AND PARAPLEGIA

Samuel I. Joseph, M.D., Ph.D.
and
Judson S. Denson, M.D., Los Angeles

The effects of various detergents left as contaminants in the needles and syringes used for spinal anesthesia were studied in experiments with 18 monkeys. There were three test groups: a series of five monkeys in which a variety of detergents were used as contaminants, a series of five monkeys in which the contaminant was a 1% solution of tribasic sodium phosphate (TSP), and a series of four monkeys in which the contaminant was 5% TSP. There was a contrast group consisting of four monkeys who were observed for five months or more after spinal anesthesia had been induced with due precautions against contamination with detergents. In this group no clinical, gross, or microscopic evidence of neurological damage was obtained. In the test groups only two monkeys escaped arachnoiditis; all the others developed it in varying degrees of severity, and one became clinically paraplegic. Detergents are not the only contaminants to be concerned about, but it is clear that extreme care should be used in all phases of the induction of spinal anesthesia.

Arachnoiditis and paraplegia after spinal anesthesia have recently been ascribed to detergent cleanser residues in the inadequately rinsed needles and syringes used for administration of spinal anesthesia.[1] It has been confirmed that this view has been based on strong circumstantial evidence without experimental verification.[2] Preliminary experimental work in monkeys, in support of the circumstantial evidence, was reported in brief from this department in 1957.[3] The present report is concerned with the continuation and expansion of the preliminary study.

Methods

The animals used were young adult male monkeys (the macaque) weighing between 3 and 10 lb. (1.3 and 4.5 kg.). The animals were put to sleep with pentobarbital (Nembutal), injected intraperitoneally; they then were subjected to spinal anesthesia with use of 1% tetracaine hydrochloride and 10% dextrose solution in varying hyperbaric combinations ranging from 2 to 4 mg. of tetracaine and 20 to 80 mg. of dextrose. The dose of tetracaine used was 2 mg. in all monkeys except two of the larger animals. Low lumbar puncture was performed with a 22-gauge needle. Spinal anesthesia was produced to various thoracic sensory levels.

The technique used for administration of spinal anesthetic drugs in the monkeys was as exactly comparable to that used in human patients as possible. In regard to the equipment used, in the control group of animals the syringes and needles used had been prepared for patients and in the experimental animals the syringes and needles had been washed in detergent solutions and then autoclaved without rinsing.

From the Anesthesia Section, Department of Surgery, University of Southern California School of Medicine, and the Department of Anesthesia, Los Angeles County General Hospital.

Read in the Symposium and Panel Discussion on Spinal Anesthesia before the Joint Meeting of the Section on Anesthesiology and the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

In the exploratory preliminary experimental group, as previously reported,[3] various detergents commonly used in hospitals for the cleansing of needles and syringes were used in varied combinations and concentrations. Two of the five monkeys

Fig. 1.—Marked inflammatory reaction in severe arachnoiditis in monkey. Note adhesion between pia and arachnoid (× 250).

in this group received single contaminated injections, one received two, one received three, and one received four.

In the present experimental group, tribasic sodium phosphate (TSP), commonly found in commercial detergent mixtures and also used by itself for similar purposes, was the only contaminant introduced (in 1 and 5% concentrations). Each animal in this group received just one injection.

At the conclusion of the observation periods, the animals were again put to sleep with pentobarbital injected intraperitoneally and the spinal cords, with intact meninges, were removed for study.

Results

Control Series.—Four animals were observed for five months and three for nine months after the induction of spinal anesthesia. No clinical evidence of neurological damage was noted, nor was gross evidence of neuropathology seen at sacrifice. Microscopic studies revealed no chronic meningeal reaction.

Preliminary Experimental Group.—Five animals in the preliminary experimental series were observed for 6 to 14 months after the initial injection. One monkey (no. 4) was observed to be clinically paraplegic four months after its first anesthesia, or two months after its second anesthesia. The onset of paraplegia was clinically abrupt, without detectable premonitory symptoms. Six months after the onset of this animal's gross hind-limb paralysis, the beginning of clinical improvement was apparent. This improvement continued over a three-month period, with slight weakness of the lower extremities remaining as the only evident residual at the time of sacrifice. The other four monkeys remained clinically normal.

Study of the spinal cords and their investments revealed arachnoiditis in all. The pathological changes were graded as "severe" in one monkey, "moderate" in two, and "mild" in the remaining two. The pathology, summarized, was as follows:

Severe Changes: Marked inflammatory reaction of subarachnoid space, with practically solid adhesion between pia and arachnoid, was observed in one monkey (no. 4), as illustrated in figure 1. There was marked thickening of the walls of blood vessels,

Fig. 2.—Severe degenerative changes in nerve fibers, with thickening about trunks and binding of roots, in monkey with experimentally produced arachnoiditis (× 250).

producing severe degenerative changes in nerve fibers associated with thickening about the trunks and binding of the nerve roots together (fig. 2), and lymphocytic infiltration of blood vessel walls. Proliferative changes in dorsal root ganglions, with chromatolytic changes in ganglion cells were also seen. There was loss of myelin in the peripheral

tissues of cord, especially of the posterior and lateral funiculi (fig. 3). Pathology was graded as 4+. The animal had received two injections.

Moderate Changes: One monkey (no. 5) had irregular thickening of the arachnoid and pia-arachnoid adhesions. Pathology was graded as 2+. The animal had received one injection.

Fig. 3.—Loss of myelin in peripheral tissues of cord (× 250).

In another animal (no. 2) with irregular thickening of arachnoid, the adhesions were all of meninges. The pathology was graded as 2+. This animal had received four injections.

Mild Changes: One animal (no. 8) showed a slight thickening of pia-arachnoid, with adhesions of nerve roots. The pathology was graded as 1+. The animal had received one injection. Another monkey (no. 1) had irregular thickening of arachnoid and nerve root demyelinization. Pathology was graded as 1+. The animal had received three injections.

No correlation could be made in this group of the extent or degree of pathology, the number of injections which each animal received, and the particular detergent used.

Present Experimental Group.—In four animals in the present experimental series spinal anesthesia was induced with use of needles and syringes contaminated with a 5% TSP solution. In two of these, sacrificed three and seven months after injection, respectively, the appearance of the spinal cords and meninges did not differ from that in the control animals. In a third animal, sacrificed three months after injection, slight hind-leg weakness was noted at the time of sacrifice. Gross observation of the meninges revealed a small (2-by-3-mm.) cyst of the dura at the site of lumbar puncture. Microscopic examination of the cord and meninges revealed minimal pia-arachnoid thickening, with some adhesion formation. In the fourth animal in this group, sacrificed three months after injection, no clinical evidence of neuropathology was noted. Examination of the cord and meninges revealed moderately severe arachnoiditis (3+), with adhesions between nerve roots, vacuolization of nerve roots (fig. 4), and marked cellular reaction in the meninges.

Five animals in the present experimental group were given an injection with needles and syringes contaminated with a 1% TSP solution. Two of these were sacrificed three months after injection, one five months after injection, and two eight months after injection. The appearance of the spinal cords and meninges of these animals did not differ from that of the control animals.

Comment

We know that serious neurological complications of spinal anesthesia were observed prior to the development and use of detergent cleansing solutions.[4] We also know that valid comparison of the incidence of such complications in the past decade

Fig. 4.—Vacuolization of nerve roots in monkey with moderately severe arachnoiditis (× 125).

with the incidence in more distant past cannot be made, particularly since incidence per se, unrelated to anesthesia, is so indefinite. However, it is difficult for us to believe that improved publicity is the only real basis for the apparent increased incidence of complications as reported in the literature, especially since this apparent increase so closely parallels the widespread use of detergents.

The great number of uncomplicated spinal anesthesias which have been recorded through the years must be regarded as attesting to the relative safety of the anesthetic drugs themselves as they are generally used in modern practice. Therefore, clinical reports of neurological complications implicating contaminants cannot be ignored.

This study should not be construed as suggesting that detergent contaminants are the only contaminants with which one need be concerned in the administration of spinal anesthesia. Many histotoxic chemicals, including antiseptics, can undoubtedly produce comparable pathology.[5] Since detergents resist rinsing, extra diligence must be applied to their removal from syringes and needles. Since alcohol is often the solvent for antiseptic solutions used for skin preparation, care must be taken to avoid contamination of gloves, needles, syringes, and ampuls by such solutions. The dangers of "wet" (i.e., immersion) sterilization with alcohol or other antiseptic solutions of ampuls of drugs used for spinal anesthesia have been well documented.

Although chemical contamination no doubt does not represent the final explanation of the problem, it is a controllable aspect of it. Still remaining to be explained are the facts that arachnoiditis and paraplegia have been found in patients who have never received any type of anesthetic drug, as well as in patients who have been under only general anesthesia.

Summary and Conclusions

Spinal anesthesia was induced in a series of nine monkeys with needles and syringes which had been washed in strong detergent solutions and then autoclaved without rinsing. Seven of the animals were shown to have arachnoiditis when they were sacrificed 3 to 14 months after injection. In two of these the arachnoiditis was severe, with one animal clinically paraplegic.

Inadequate rinsing of hurriedly prepared detergent solutions, which can so readily be made far stronger than necessary, has been postulated as a hospital situation which can result in detergent contamination of solutions used for spinal anesthesia. Beginning with the care and cleansing of needles and syringes, extreme care must be observed in all phases of the induction of spinal anesthesia in order to avoid introducing potentially histotoxic substances into patients.

1200 N. State St. (33) (Dr. Denson).

We acknowledge with gratitude the contributions of Drs. Cyril B. Courville, neuropathology consultant, and John S. Marsh and Allan M. Warner, neurosurgery consultants.

This study was supported by grants from Ciba Pharmaceutical Products, Inc., Burroughs Wellcome & Co., Inc., and the Attending Staff Association of the Los Angeles County General Hospital.

References

1. Winkelman, N. W.: Neurologic Symptoms Following Accidental Intraspinal Detergent Injection, Neurology **2**:284-291 (July-Aug.) 1952. Winkelman, N. W.; Gotten, N.; and Scheibert, D.: Localized Adhesive Spinal Arachnoiditis: Study of 25 Cases with Reference to Etiology, Tr. Am. Neurol. A. **78**:15-18, 1953. Paddison, R. M., and Alpers, B. J.: Role of Intrathecal Detergents in Pathogenesis of Adhesive Arachnoiditis, A. M. A. Arch. Neurol. & Psychiat. **71**:87-100 (Jan.) 1954.

2. Winkelman, N. W.: Personal Communication to the authors. Paddison, R. M.: Personal Communication to the authors.

3. Denson, J. S., and others: Effects of Detergents Intrathecally, Anesthesiology **18**:143-144 (Jan.-Feb.) 1957.

4. Courville, C. B.: Untoward Effects of Spinal Anesthesia on Spinal Cord and Its Investments, Anesth. & Analg. **34**:313-333 (Nov.-Dec.) 1955.

5. Hurst, E. W.: Adhesive Arachnoiditis and Vascular Blockage Caused by Detergents and Other Chemical Irritants: Experimental Study, J. Path. & Bact. **70**:167-178 (July) 1955.

EFFECT OF ALTITUDE ON ASTHMA.—Patients with asthma may fly, preferably in pressurized planes, using the criteria with which the examining physician is best acquainted. Chronic bronchitis, asthmatic bronchitis, and bronchiectasis, unless severe, do not bar flying but moderate pulmonary emphysema might do so, particularly in the presence of large blebs. Patients who have dyspnea at rest on the ground will probably not find their symptoms aggravated at altitudes in pressured aircraft. Asthmatic patients sensitive to pollens may find some relief even though flying during their particular pollen season, but should not fly during an acute asthmatic attack. Vital capacity, in itself, should probably be above 50 per cent of the calculated value. While oxygen and various types of bronchodilators could be made available to passengers, the particular medication, as prescribed by a physician and with which the patient is familiar, is to be preferred. Prophylactic treatment prior to flight may help prevent attacks. Hyperventilation particularly during an initial trip by air, must be distinguished from asthma and this is at times quite difficult to do. Cyanosis, if present, without further consideration is sufficient in itself to keep a patient out of the air.—S. W. Simon, M.D., The Effect of Altitude on Asthma, *The Journal of Aviation Medicine*, June, 1958.

IS HEAT STERILIZATION OF LOCAL ANESTHETIC DRUGS A NECESSITY?

L. Donald Bridenbaugh, M.D.
and
Daniel C. Moore, M.D., Seattle

Heat sterilization of all local anesthetic drugs and equipment is mandatory but is not being generally practiced. A survey of the techniques observed in using local anesthetic drugs showed that only 33 out of 101 hospitals were autoclaving the solutions before use. The remaining 68 hospitals depended on cold sterilization, the immersion of the ampul, vial, or bottle in a germicidal solution which acts upon the outside but not on the contents. Experience with 17,368 regional block procedures over a 54-month period has led the authors to conclude that a careful technique which includes the autoclaving of the anesthetic in its container is mandatory. The procedure here described is based on the demonstration that the local anesthetics most commonly used can be autoclaved for 30 minutes at 255 to 260 F. and 18 to 20 lb. of pressure (124 to 127 C and 1.22 to 1.36 atmospheres above ambient pressure) without significant loss of potency. This reduces the danger of bacterial contamination and simplifies both the preparation of regional block trays and the execution of regional block anesthesia.

The assurance that a local anesthetic solution as well as the equipment employed for its injection is free from contamination prior to performance of a regional block procedure has always been a concern to the physician using these techniques. Heat sterilization of the equipment is now a standard procedure. Unfortunately, there is a misconception that the potency of drugs used to prepare a local anesthetic solution is markedly decreased by heat sterilization. Furthermore, such drugs or solutions purchased in vials or bottles are assumed to be sterile as received from the pharmaceutical firm. Therefore, "cold" sterilization or no resterilization of these drugs prior to injection is the usual routine in many hospitals throughout the United States today.

Cold sterilization is the immersion in antiseptic solutions, e. g., 70% alcohol, of the ampuls, vials, and bottles of drugs and solvents necessary to perform a regional block technique. Cold sterilization is employed primarily to check ampuls of drugs for cracks in the glass which may occur during handling and to sterilize the outside of the ampuls so that they may be placed on a tray that has been sterilized with heat.

It is the purpose of this paper to show evidence that cold sterilization or no resterilization is the routine in many hospitals, to point out the disadvantages of cold sterilization, and to describe the advantages and method of heat sterilization as it is used by us. Furthermore, in our opinion, this study proves that heat sterilization of drugs and equipment under the direction of the physician who is to use them is mandatory.

Method of Study

A questionnaire was sent to all the hospitals in the state of Washington in August, 1957. The questionnaire asked which local anesthetic drugs were used in that hospital; how the drugs were sterilized; and, if cold sterilization was used, which solutions were used. Furthermore, the records of patients to whom regional blocks were administered at the Mason Clinic were reviewed from October, 1953, the date on which we changed from cold sterilization to heat sterilization, to March, 1958.

From the Mason Clinic.

Read in the Symposium and Panel Discussion on Spinal Anesthesia before the Joint Meeting of the Section on Anesthesiology and the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Results

Of the 121 questionnaires sent to the hospitals, 101 (83.5%) were returned. Of this number only 33 hospitals reported they were autoclaving the drugs used for spinal anesthesia; the remaining 68 hospitals used cold sterilization. The agent used was benzalkonium (Zephiran) chloride, 1:1,000, in 25 hospitals; alcohol in 14; methyldodecylbenzyl trimethyl ammonium chloride solution (C. R. I. germicide) in 5; potassium-mercuric-iodide solution in 2; and miscellaneous in 22. Only two hospitals reported they were autoclaving the multiple-dose rubber-stoppered vials or bottles containing the local anesthetic solutions used for infiltration, field block, caudal block, epidural block, or peripheral nerve block; in the remaining 99 hospitals these multiple-dose vials and bottles were used as received from the pharmaceutical company.

A review of our records indicated that 17,368 regional block procedures had been done since October, 1953 (see table). There was not a single

case of infection or neurological sequelae in any of these cases which could be blamed on the use of unsterile equipment or a contaminated local anesthetic solution.

Regional Block Anesthesias Done at the Mason Clinic from October, 1953, to March, 1958

Procedure	Oct.-Dec., 1953	1954	1955	1956	1957	Jan.-March, 1958	Total
Peripheral nerve block	298	1,087	1,002	971	934	276	4,623
Subarachnoid (spinal) block	137	542	515	628	667	190	2,679
Caudal block	227	1,294	1,523	1,833	2,606	523	7,436
Segmental spinal Epidural block	134	569	534	591	674	128	2,630
Total	796	3,492	3,634	4,023	4,811	1,117	17,368

Comment

The results of the questionnaire survey confirmed our belief that, in a large number of the hospitals in the state of Washington, the ampuls, vials, or bottles of local anesthetic drugs and/or solutions for regional block procedures were not being autoclaved prior to use. It was surprising that so many workers were still using cold sterilization for spinal anesthetic drugs.

Heat sterilization has the following advantages over cold sterilization [1]: 1. The drugs, together with the syringes, needles, and necessary equipment, can be sterilized in the block trays. This avoids the opportunity for contamination by use of an unsterile pick-up forceps for transferring the ampul from the jar to the block tray or use of an unsterile file for opening the ampul. Also, it avoids dripping of the sterilizing solution onto the equipment to be used for the block.

2. The possibility of a contaminated solution dispensed by the manufacturer is eliminated.

3. Heat colors, dissolves, or evacuates the crystals or solution of the local anesthetic drug or other agent should there be a small, invisible crack in the sealed ampul. The neurolytic solutions employed in cold sterilization can gain entrance into the ampul in small quantities not detectable even though no discernible cracks are found in the ampuls.

4. Gummed labels are sterilized. This is not true when cold sterilization is used, since the antiseptic solution does not penetrate through gummed labels used to identify ampuls or under rubber bands used to hold ampuls together.

5. Last, but probably most important, heat sterilization forestalls the legal charge of neglect. The most convincing argument for heat sterilization of local anesthetic drugs was in the legal decision of Wooley and Roe versus Ministry of Health of Great Britain, Dr. Graham, and others.[2] In this case two men, who were paralyzed after spinal anesthesia, were suing for negligence because the physician administering the subarachnoid block had soaked the ampuls in phenol prior to use instead of autoclaving them. During the trial, Dr. MacIntosh testified that in 1953 the best way of sterilizing ampuls was by autoclaving. Lord Justice Denning stated, "Dr. Graham sought to escape the danger of infection by disinfecting the ampoule. . . . He did not know that there could be undetectable cracks, but it was not negligent for him not to know it at that time. We must not look at this 1947 accident with 1954 spectacles. . . . But we have been warned . . . and to keep ampoules in solution, until further evidence is forthcoming, in the future will be regarded legally, as negligence."

Because of the literature extolling the virtues of heat sterilization and because this legal decision was well known, the following routine for cleaning and sterilization of equipment, drugs, and solvents used to prepare local anesthetic solutions was established in our institution in October, 1953.[3]

1. The needles, syringes, and solution cups are washed with copious amounts of clear tap water and rinsed with ether. Detergents are not used.[4] 2. The stainless steel trays for regional block anesthesia, containing the equipment, drugs, and solvents, are prepared (fig. 1). 3. A sterilizer control (Diack) is placed in each tray as it is wrapped. 4. The trays are then autoclaved at 225 to 260 F under 18 to 22 lb. of pressure for 30 minutes.

5. When the tray is dry it is removed from the autoclave and stored on a shelf away from all solutions. This point is stressed, for if solutions are unsuspectedly spilled on the tray it may become contaminated even though the sterilizer control in the tray shows adequate sterilization when it is checked (fig. 2). 6. Reserve ampuls of drugs for all regional block procedures are placed in test tubes which are sealed. Extra bottles of saline solution and

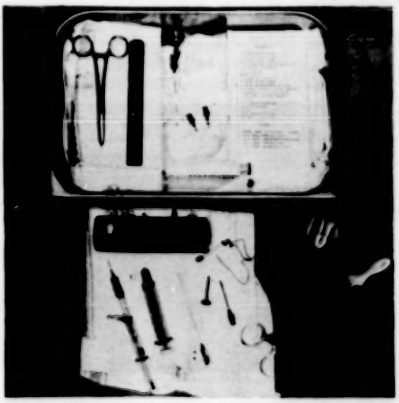


Fig. 1.—Stainless steel tray for regional block anesthesia, containing equipment, drugs, and solvents necessary for subarachnoid block.

vials of commercially prepared local anesthetic solutions too large to fit in test tubes are wrapped individually, together with a sterilizer control, and heat sterilized. Both test tubes and wrapped bottles and vials are stored in a special cabinet (fig. 3). Thus, sterile drugs, solvents, and commercially prepared local anesthetic solutions are always available to replace ampuls in the block trays which have been broken or have evaporated.

We never use hospital-prepared solutions for any regional block procedure. Even the commercially prepared solutions are autoclaved prior to use. Furthermore, all multiple-dose vials are resterilized after being used and before the remaining solution is injected into another patient. Although very few of our colleagues observe this practice and have ridiculed us for this added precaution, its importance was impressed on us in March, 1958, when we received a shipment of 50-cc. multiple-dose ampuls of a local anesthetic solution which had somehow slipped out of the drug company without being sterilized. This was not recognized by the pharmaceutical house until the drug had been in our possession for a number of days. Had this drug been used without our autoclaving it, the troubles it could have created are obvious.

Our experience has shown that the following drugs can be autoclaved at 255 to 260 F under 18 to 20 lb. of pressure for 30 minutes at least once without sufficient loss of potency to alter the expected clinical results: tetracaine (Pontocaine) hydrochloride crystals; tetracaine, 1% solution; procaine (Novocain) hydrochloride crystals; procaine, 1 and 2% solutions; propoxycaine (Blockain)

Fig. 2.—Storage space for sterilized trays for regional block anesthesia. Note separate enclosed cubicles to prevent contamination of trays by solutions unsuspectedly spilled on them.

hydrochloride, 2% solution; piperocaine (Metycaine) hydrochloride, 1.5% solution; chloroprocaine (Nesacaine) hydrochloride, 1, 2, and 3% solutions; ephedrine sulfate; methamphetamine (Methedrine) hydrochloride; methoxamine (Vasoxyl) hydrochloride; epinephrine (Adrenalin), 1:1,000; phenylephrine (Neosynephrine) hydrochloride; 10% dextrose solution; dibucaine (Nupercaine) hydrochloride; and lidocaine (Xylocaine), 1 and 2% solutions.

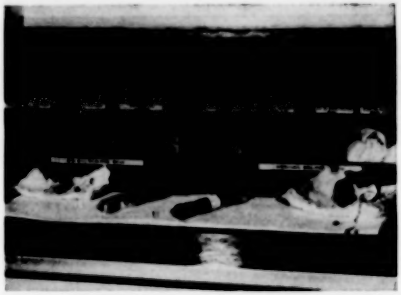


Fig. 3.—Enclosed storage cabinet for test tubes containing reserve ampuls of regional block drugs.

Ammonium sulfate (Dolamin) solutions, oil solutions for local anesthesia (such as Proctocaine), and absolute alcohol can be heat sterilized.[14] Hyaluronidase cannot be autoclaved at all. Most laboratory tests have demonstrated that the potency of the local anesthetic drugs and solutions, as well as that of vasoconstrictor drugs, is decreased slightly after one or two heat sterilizations, but this small decrease does not affect the clinical results of the drug.[5] On the other hand, more than one or two sterilizations may cause marked decrease in potency, but most figures as to the amount of decrease do not agree.[6]

Summary and Conclusions

If the practice of medicine in the state of Washington can be considered representative of the practice in the United States, then the results of a poll taken in August, 1957, would show how few physicians today appreciate the necessity for heat sterilization of all local drugs, solvents, commercially prepared local anesthetic solutions, and equipment.

The system of heat sterilization used by us in preparing drugs and equipment for regional block procedures has been successful in simplifying the preparation of regional block trays as well as the execution of regional block procedures. The danger of bacterial contamination has been reduced and the danger of antiseptic solution entering a cracked ampul eliminated. Should a neurological complication occur, at least these possible causes have been automatically eliminated. Considering the finality and seriousness of complications after regional block procedures, particularly subarachnoid block, and the large court judgments which have been awarded recently, we conclude that all the local

anesthetic drugs, solvents, and commercially prepared local anesthetic solutions, as well as equipment, should be heat sterilized under the direction of the responsible physician prior to their use if freedom from contamination is to be assured.

1118 Ninth Ave. (Dr. Bridenbaugh).

References

1. (*a*) Walton, F. A.: Correspondence, Anesthesiology **13**:441 (July) 1952. (*b*) Carter, A. B.; Hebert, C. L.; DeWald, W. S.; and Talley, A. W.: Multiple Autoclaving of Drugs Used in Spinal Anesthesia, ibid. **15**:480-483 (Sept.) 1954. (*c*) Steinberg, B. L.: Ampule Contamination in Spinal Anesthesia, ibid. **11**:257-258 (March) 1950. (*d*) Whittet, T. D.: Effect of Autoclaving on Ampoules of Local Analgesics, Anæsthesia **9**:271-280 (Oct.) 1954. (*e*) Searles, P. W., and Nowill, W. K.: Role of Sterilizing Solution in Cauda Equina Syndrome Following Spinal Anesthesia, New York J. Med. **50**:2541-2544 (Nov. 1) 1950. (*f*) Walter, C. W.: Disinfection of Ampuls, J. A. M. A. **142**:1009 (April 1) 1950. (*g*) Nicholson, M. J., and Eversole, U. H.: Neurologic Complications of Spinal Anesthesia, ibid. **132**:679-685 (Nov. 23) 1946. (*h*) Lewis, L. W.: Storing Ampuls for Spinal Anesthesia, Correspondence, ibid. **153**:50 (Sept. 5) 1953. (*i*) Spinal Anæsthetics Appeals Fail, Medico-Legal, Brit. M. J. **1**:940 (April 17) 1954. (*j*) Contaminated Spinal Anesthetic, Medico-Legal, ibid. **2**:1165 (Nov. 21) 1953.

2. Reference 1*i* and *j*.

3. Moore, D. C.: Complications of Regional Anesthesia, Springfield, Ill., Charles C Thomas, Publisher, 1955.

4. Winkelman, N. W.: Neurologic Symptoms Following Accidental Intraspinal Detergent Injection, Neurology **2**: 284-291 (July-Aug.) 1952.

5. Massa, D. J.: Autoclaved Epinephrine and Spinal Anesthesia, J. A. M. A. **157**:843 (March 5) 1955. References 1*a*, *b*, *d*, and *e* and 3.

6. Gerlich, N. A.; Nicholes, P. S.; and Ballinger, C. M.: Heat Sterilization of Spinal Anesthesia Ampuls, abstracted, Anesthesiology **18**:164-165 (Jan.-Feb.) 1957. Reference 1*b* and *d*.

ELECTROMYOGRAM IN EVALUATION OF NEUROLOGICAL COMPLICATIONS OF SPINAL ANESTHESIA

Albert A. Marinacci, M.D.
and
Cyril B. Courville, M.D., Los Angeles

Some assume that spinal anesthesia is responsible for the development of any concurrent neurological manifestations. Of 482 patients whose neurological complaints seemed to be related to spinal anesthesia, 478 showed neurological complaints due to some other concurrent and entirely unrelated conditions imitating actual complications of the spinal anesthetic agent. In the majority of instances, the causative disease proves to be either an infectious neuronitis or a peripheral neuropathy. The electromyogram plays a fundamental role in the evaluation of these complications. Differentiation in the two groups of lesions is based on the following two basic elements: (1) the distribution of the denervation, that is, electromyographic changes, and (2) the time in which the denervation activity is first detected electromyographically. The prevention of misunderstanding about spinal anesthesia is of great importance.

Muscular weakness or actual paralysis, with concomitant root pains, sometimes follows the administration of spinal anesthesia. The implications involved in this situation are so serious as to demand immediate and careful diagnostic attention. Because of the ever-increasing consciousness on the part of the public that legal action often results in large awards, anesthetists, surgeons, and hospital administrators must always be on their guard to evaluate correctly the cause in each individual case. This situation almost invariably produces a tense emotional atmosphere which leads the patient to blame either the anesthetist or the surgeon for the complications. This is especially the case if there is any delay in accounting for the paralysis. When, after surgery with use of spinal anesthesia, the patient is paralyzed in one or both lower extremities, the following questions present themselves: 1. Is the resulting paralysis a genuine motor disability or is

From the Department of Electromyography, University of Southern California, and the Los Angeles County Hospital (Dr. Marinacci), and the Division of Nervous Diseases, College of Medical Evangelists, and the Laboratory of Neuropathology, Los Angeles County Hospital (Dr. Courville).

Read in the Symposium and Panel Discussion on Spinal Anesthesia before the Joint Meeting of the Section on Anesthesiology and the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

it to be accounted for on a psychogenic basis? 2. If the paralysis is the result of a true nerve lesion, is such lesion located in the spinal cord, the spinal nerve roots, the corresponding plexus, or the peripheral nerves? 3. If such lesion is located in the spinal cord and/or the spinal nerve roots, is the anesthetic agent its actual cause or is it due to some preexisting or concurrent but unrelated disease? 4. If, on the other hand, the symptoms and signs point to the nerve plexuses and/or the peripheral nerves, is there but one nerve affected (mononeuropathy) or are several of the peripheral nerves involved (polyneuropathy)? 5. Can the etiology be proved with reasonable medical certainty? 6. Can one determine whether the mononeuropathy and/or the polyneuropathy occurred before, during, or after the spinal anesthesia was given? If one can be certain of the exact location as well as of the time of onset of the disease, one can usually come to a correct conclusion and, hence, whether it is actually a complication due to the spinal anesthetic agent or to the surgical procedure.

It is therefore fundamental to the problem to establish these facts. It is just at this point that the electromyogram becomes a useful adjunct to the investigation, as pointed out by Weddell and coworkers in 1944,[1] one of us in 1955,[2] Buchthal in 1957,[3] and Eaton and Lambert in 1957.[4] This has been proved in the past few years, when the electromyogram was used to evaluate a large series of patients of this type presumed to be suffering from postanesthesia neurological complications. Experience derived from a study of these cases clearly indicates that often what were apparently postanesthesia complications were actually due to other concomitant lesions.

In this study, we propose (1) to note the medicolegal aspects of alleged postanesthesia and postsurgical neurological complications, (2) to review briefly what is known about the cause and effects of true neurological complications of spinal anesthesia, (3) to point out the nature of certain simulators of postanesthesia complications particularly of acute infectious neuronitis, (4) to show how the electromyogram is of value in distinguishing between true complications and such imitators, and (5) to indicate the double aspect of spinal anesthesia complications.

Medicolegal Aspects

Out of thousands of patients who have had spinal anesthesia, one may have a profound neurological complication, such as paraplegia of both lower extremities with loss of sphincter control. This rare calamity has created a state of apprehension in medical attendants, including anesthetists, surgeons, consultants, hospital attendants, and administrators, as well as in the general public and, in particular, the patient himself when spinal anesthesia is involved. This situation comes to light whenever any degree of muscular weakness or paralysis follows an operation on a patient under spinal anesthesia, whether these motor symptoms are psychological or pathological in origin. It is clear that, in some cases, the spinal anesthesia has been erroneously incriminated even though a paralysis, such as a foot drop, has occurred weeks after the patient has been discharged from the hospital.

The genuine complications, although rare, have created fertile soil for the unscrupulous members of the legal profession to take advantage of the dictum *res ipsa loquitur*. The anxious patient who finds himself with either muscular weakness or paralysis after spinal anesthesia will naturally ask the doctor what has happened. He complains, "I walked into the hospital and, after the surgery, I am now unable to move my legs." The embarrassed surgeon, as well as the consultant, usually finds it difficult to give the patient a satisfactory answer. In an attempt to answer the patient's inquiry, the surgeon may say, "Possibly I damaged a nerve at surgery; your paralysis may be the result of the spinal anesthesia; you have developed poliomyelitis; or you are imagining your paralysis." The seeds of uncertainty are thereby planted in the minds of the patient and his family. It is usually not difficult to find a member of the legal profession who consciously or unconsciously waters the ground now well fertilized by the already emotional situation. This creates a crop of evil results for the patient, because of lack of proper diagnosis and prognosis, with failure to institute proper treatment. The doctor should learn to say, "We shall find out, but at the present time I do not know." This more positive approach would make the patient more cooperative with the doctor in arriving at the proper diagnosis and proper treatment. It is even possible in most instances to give a favorable prognosis.

This situation can be solved in most cases by the doctors' refraining from expressing divergent opinions and speculative diagnoses and by their securing proper neurological advice and the help of a competent electromyographer. In most instances, the simulators of complications of spinal anesthesia can promptly be brought to light. Such a distinction will benefit most of the patients in that the correct diagnosis and, eventually, full recovery can be achieved.

Pathology of Intraspinal Complications

It has been clearly shown by one of us [5] that certain complications affecting the meninges, nerve roots, and the spinal cord may occur as a result of spinal anesthesia. Although such complications are relatively rare, at least in the United States, the residuals are so serious as to demand careful attention by the anesthetists. It is still uncertain whether these complications are the result of a concentration of the anesthetic agent or whether they occur as a consequence of an irritative product (detergent) injected into the spinal canal along with the

anesthetic drug. The number of reported cases in which the intraspinal lesion has been verified at operation or at autopsy is still relatively small. From verified cases, however, it has been shown that the lesions responsible for the clinical symptoms are somewhat variable.

Cauda Equina Syndrome.—The cauda equina syndrome is characterized by a permanent paresis or paralysis of the bladder and/or rectal sphincters associated with persistent impairment of sensation of the perineal region. In acute cases, the local meninges and nerve roots are observed to be swollen and markedly congested and the nerve fibers of these roots show early degeneration in the form of vacuolization, as shown by Ferguson and Watkins in 1938.[6] The causative lesion, as ultimately found at autopsy by one of us (C. B. C.), has been marked atrophy of the lower nerve roots of the cauda equina. There is some uncertainty as to whether an isolated peripheral neuropathy can actually occur as a complication of spinal anesthesia. While this cannot be entirely excluded, the possibility of such a neuropathy being due to some other coincidental disease seems to be more likely. Local adhesions of the meninges to the roots of the cauda equina may also be present and found to involve higher levels of the spinal cord.[5]

Chronic Radiculitis.—Multiple chronic radiculitis as a consequence of spinal anesthesia is probably more common than is appreciated. The development of arachnoidal adhesions can evidently be a slow process, as in this condition, resulting from other causes. Weeks or even months after the spinal anesthesia, the patient begins to experience root pains, often scattered at various levels of the spinal cord. Radicular pain, focal paralysis, and atrophy are the common clinical complaints, with motor root involvement being verified by the electromyogram. The lesion begins apparently as an aseptic meningitis which may either clear up spontaneously within two weeks or continue as a chronic form with adhesion formation, as pointed out by Thorsen in 1947.[7] The presence of such adhesions is usually verified by exploration. Both the subdural and subarachnoid spaces may be obliterated with thickening of the meninges.[8]

Myelopathy.—Myelopathy after spinal anesthesia constitutes the most serious type of complication as far as the lesion is concerned, being manifest clinically by paraplegia of variable degrees with anesthesia more or less complete up to the level of the cord damage. At times the level may be betrayed by irritative root manifestations. However, multiple foci of root damage may be found by the electromyogram. There are two possible postanesthesia spinal cord lesions: (*a*) acute and (*b*) chronic. The acute lesion may be due in part to severe shock; this seemed to be the chief cause of death in one case as verified by one of us.[5] The lesion proved to be an acute total necrosis of the gray matter of the spinal cord. Such lesions must be extremely rare, for no reports of similar cases have come to our attention.

Chronic myelopathy resulting from spinal anesthesia is a pathological complex with both primary and secondary pathogenic factors. It seems obvious that the external adhesions with involvement of the spinal roots are the direct and immediate effect of the agent (or some concomitant substance) on the limiting leptomeninges with thickening and opacity of this membrane. This process is manifest visibly by the formation of adhesions which bind the arachnoid to the pia mater and to the dura mater. Externally, it seems able also to provoke an inflammatory reaction of the dura, with thickening of this membrane. As the process tends not only to spread to higher levels of the cord but also to become accentuated by the contraction of the scar, the disordered local circulation leads to secondary damage of the underlying nervous tissues themselves. The occurrence of peripheral demyelinization of the spinal cord was first demonstrated experimentally by Spielmeyer in 1908[9] and verified in man by one of us in 1955.[5] It is possible that this is a transitory and reversible phenomenon, a possible functional disturbance in the external circulation. Ischemia of the tissues leads to softening of the peripheral portions of the cord, as shown by Brock and associates in 1936,[10] with replacement gliosis if the damage is incomplete. This process seems to be the result of changes in the arterial blood supply, possibly initiated by vasospasm, but ultimately it is due to structural changes in the arterial wall—"necrosing arteritis."[11] Perhaps facilitated by the pulsating action of the fluid column on the softened and immobilized spinal cord, central cyst formation develops on the disintegrating cerebral gray matter, adding further to the picture of gross disability.

Although the pathogenesis of the ultimate effects of spinal anesthesia is not completely understood, there can be no doubt that serious irreversible lesions sometimes result. Whether it is the effect of the anesthetic agent itself or of some irritant (alcohol, soap, or detergent) introduced with it is not yet clear. The fact remains that the clinical symptoms as well as the physical effects indicate that the earliest changes are to be expected in the spinal nerve roots, especially those of the cauda equina, with fairly obvious typical pain and a peripheral type of motor disability (weakness and atrophy). It is for this reason that the use of electromyography is of such importance in the early evaluation of an actual or alleged complication. After the secondary and delayed effects of cord involvement become manifest, the diagnosis is rarely in doubt.

Simulators

In this present investigation it has been shown that, with the aid of the electromyogram, many conditions may be concurrent during the period of

surgery with use of spinal anesthesia. Such disorders have given rise to symptoms which often simulate or imitate the actual complications of spinal anesthesia. These simulators have almost invariably misled the clinician to incriminate the spinal anesthesia as the cause of the neurological manifestations. These simulators will be discussed in the following paragraphs in the order of their similarity to the problem. They are as follows: (1) acute infectious neuronitis or polyneuritis, (2) preexisting pressure neuropathy, (3) traumatic nerve injury as a direct result of surgery, (4) pressure on the nerve either while the patient is on the operating table or during the period of recovery, (5) pressure neuropathy while the patient is convalescing in the hospital or at home, (6) toxic plexitis, particularly that due to horse serum reaction, (7) progressive spinal muscular atrophy, (8) the myopathies and myotonia, (9) recurrent multiple sclerosis, (10) disuse atrophy, and (11) hysteria.

Acute Infectious Neuronitis.—As one of us and Rand reported in 1956,[12] acute infectious neuronitis can be a perfect imitator of lesions residual to spinal anesthesia. This is because neuronitis is an inflammation of the entire neuron, including the nerve roots and the nerve cells within the spinal cord. Because the anesthetic agent also affects these structures, it is not difficult to understand the similarity of symptoms.

Neuronitis can produce both a reversible and an irreversible reaction in the neuron. In the reversible transitory state, the manifestations can be of three types: (1) pure sensory, (2) pure motor, and (3) sensory and motor combined. In this reversible state, the mild inflammatory reaction and vascular changes probably produce an edema. However, the insult is not sufficiently severe to produce destruction of the nerve cells or of its axons. Therefore, within a period of days the patient has fully recovered. The disease in such a case produces only a transitory physiological block and manifests itself in the form of pure sensory, pure motor, or a combination of both phenomena. The sensory symptoms are manifested by severe radiating pain in the corresponding dermatome. If the disease occurs at the midthoracic level, the resulting pain may simulate that of acute gallbladder disease or peptic ulcer. If the disease attacks the lower thoracic nerve roots, it can simulate either an acute appendicitis or an acute intestinal disorder. If the upper lumbar roots are affected, a surgical lesion of the kidneys is suggested. If the lower lumbar or sacral roots are involved, the acute pain in the lower part of the back naturally imitates a lumbar herniated disk. Perhaps another reason for the resemblance to spinal anesthesia complications is the tendency for both conditions to affect the lower group of spinal nerve roots rather than those of the upper thoracic and cervical ones. This confusion of entities probably accounts for a variety of cases in which the surgeon is disappointed at surgery to find little or no gross changes to account for the severe symptoms. If the operation is done and the spinal anesthesia given when the changes incidental to neuronitis are reversible, it is to be assumed that a natural course of recovery follows. This will occur in patients with the combination of sensory and motor phenomena, as well as in those with either the sensory or the motor phenomenon alone.

On the other hand, when the sensory-motor combination is due to an irreversible lesion, that is, when the disease has produced a degree of actual degeneration of the cells and their axons, the situation will be much more serious. The severe pain will continue and will be followed by paralysis. When this takes place during the postoperative period when the anesthetic agent should be wearing off, the persistence of paralysis raises the question of its origin in the anesthetic agent.

Another serious aspect of this disease is when the infection involves the medullary substance of the spinal cord, producing a form of myelitis, in which case the total picture is then identified as a neuromyelitis. Less frequently, the inflammation also affects the brain itself; this is referred to as neuromyeloencephalitis. These cases are usually fatal. One case in particular during its sensory phase presented acute local symptoms of a typical L-4 herniated disk. The opaque myelogram showed some defect, supporting the diagnosis of such a lesion. However, routine electromyographic evaluation showed, instead of a nerve root compression, diffuse changes from head to foot, including the cranial nerves, all the paraspinal muscles from C-2 through S-5, and all four extremities. Because of the electromyographic findings, the contemplated laminectomy with use of spinal anesthesia was postponed. Within two days, the patient became completely paralyzed. This was followed by central respiratory difficulties. The patient survived in a respirator for two weeks and finally died. If the laminectomy with spinal anesthesia had been done as contemplated, certainly the paralysis and rapidly progressive course which followed would have been attributed to a tragedy of spinal anesthesia complications. It is apparent that when this has happened it has been reported in the literature as acute necrosis of the central gray matter as a possible type of complication of spinal anesthesia.

Clinically, acute infectous polyneuritis resembles grossly a neuronitis. However, there can be one main specific difference between the two: the spinal fluid protein level is normal in polyneuritis while in neuronitis it is usually elevated with a normal cell count. Although the electromyographic changes vary in these disease entities, that is, in neuronitis the paraspinal muscles are involved in addition to the lower extremities and in polyneuritis only the lower extremities are involved, nevertheless when

the paralysis is limited to one or both lower extremities it is also a perfect imitator of the complications of spinal anesthesia.

Preexisting Pressure Neuropathy.—Pressure neuropathy can occur before the patient comes to the hospital. He may have been either under the influence of drugs or alcohol or in an unconscious state due to various causes. This situation results in a complete relaxation of the muscles, thus leaving the nerves unprotected and producing an ideal condition for pressure neuropathy. Certain nerves are liable to pressure because of their anatomic accessibility. For example, the leg hanging over the side of the bed exerts pressure on the sciatic nerve. Prolonged crossing of the legs exerts pressure on the peroneal nerve at the head of the fibula. When the leg is dangled over a chair, pressure is created on the tibial nerve at the popliteal fossa. Overabduction can stretch the obturator nerve at its bony emergence. When the patient hangs an arm over a chair, pressure is exerted on the ulnar and median nerves at the middle of the arm. The presurgical neuropathies have been encountered in acute gastric conditions, such as perforated peptic ulcer, pancreatitis, acute gallbladder disease, acute intestinal obstruction, acute appendicitis, such gynecologic conditions as ectopic pregnancy, and induced abortion with profuse bleeding. An undetectable paralysis, already present, becomes apparent as the patient recovers from surgery. The persistence of the paralysis is usually alleged to be the result of a complication of spinal anesthesia.

Traumatic Nerve Injury.—Traumatic nerve lesions as a direct result of surgery have been observed in a few patients.[13] A few cases have been seen of the nerve being actually damaged during surgery but which imitated the complications after spinal anesthesia. The femoral nerve was severely damaged during hernia repair in two patients. This nerve has been partially damaged in eight cases during pelvic surgery. The paralysis in these cases not being present before surgery, the spinal anesthesia has invariably been incriminated for the neurological complication. If the lesion is preexistent, the denervation will be present during the first two postoperative weeks. If this paralysis is the result of the surgical procedure, the changes will not appear until 21 days after surgery. A partial nerve lesion can be demonstrated with the aid of the electromyogram in the presence of complete paralysis. Such favorable information gives the patient a considerable amount of psychological relief when he is informed that the paralysis is not a complication of spinal anesthesia, that the nerve was not cut during surgery as was possibly suggested by medical attendants, and that he will eventually recover from his paralysis. This favorable information has usually dissipated any contemplated medicolegal action.

Pressure Neuropathy During Surgery.—Pressure on the nerve during the period of surgery and/or recovery period has been observed rather frequently.[13] In this condition, denervation activity will be limited to the muscle group innervated by the affected nerve. The electromyographic changes will appear in the fourth postoperative week. Here again, these pressure neuropathies have imitated the complications of spinal anesthesia, but the distribution of electromyographic changes are those of a mononeuropathy and not those of cauda equina radiculopathy. The nerve lesion which most resembles the complication is that of the sciatic nerve caused by either intramuscular injection in the gluteal region or pressure at the gluteal fold. Both femoral and obturator nerves have been found to be liable during extreme abduction during vaginal or rectal procedures. Also, the obturator nerve has been found stretched when the leg was allowed to be in an extreme abductive position while the patient was in an unconscious state. The peroneal nerve is liable to pressure at the head of the fibula, resulting in a foot drop. Cases have been seen in which pressure on the tibial nerve at the popliteal fossa has occurred, resulting in muscular weakness and atrophy of the calf and foot. In addition, bilateral pressure on the ulnar nerve resulting in muscular wasting of both hands brings a cervical or upper thoracic lesion into consideration and has simulated chronic adhesive arachnoiditis.

The electromyographic changes in all these cases are to be found three weeks after the actual date of the surgery. However, one can not definitely state whether such pressure took place one or two days before, during, or immediately after surgery. One can definitely state that the affection is not the result of the surgical procedure if such a lesion is not within the area of the surgery, such as a peroneal nerve involvement (foot drop) after abdominal surgery. On the other hand, the spinal anesthesia in these cases cannot be incriminated, regardless of the date of appearance of the electromyographic changes, for the simple reason that the paraspinal muscles are normal.

Pressure Neuropathy During Convalescence.—Pressure neuritis during the convalescent period can occur either in the hospital or after the patient returns to his home.[14] The muscular weakness or paralysis has been alleged to be the direct result of spinal anesthesia complication. This type of neuropathy often occurs when the patient stays in bed reading for long periods of time; the exertion of pressure at the elbows produces changes in the ulnar nerves, resulting in muscular wasting of the hands. Occasionally, this condition has been interpreted clinically as the progressive widespread spinal cord changes which are seen in chronic progressive adhesive arachnoiditis.

Patients have also been observed who had peroneal and tibial nerve lesions resulting from either prolonged crossing of the legs or dangling of the legs while sitting in a rocking chair in the hospital or at home (viewing television). Here again the spinal anesthesia has been incriminated.

Toxic Plexitis.—Toxic plexitis is most frequently the result of a horse serum reaction from tetanus antitoxin injection. However, occasionally it is seen in other toxic reactions after an extremely high fever. The factor in this lesion which simulates the complications of spinal anesthesia is that the clinical muscular weakness or paralysis does not appear until about 10 days after the injection. Patients who have had surgery under spinal anesthesia during this intermediate period and whose paralysis appears during the postoperative period have erroneously incriminated the surgical or spinal procedure for the neurological complications. This has been especially true when the reaction was severe, involving not only the cervical and brachial plexuses but, to lesser degree, the lumbosacral plexuses as well. In these cases, the electromyographic changes are essentially peripheral, with no specific changes in the paraspinal muscles. This characteristic distribution rules out the complications due to the anesthetic agent, regardless of the time when the electromyographic changes are detected. When this condition is unmasked, naturally the patient who is apprehensive about the complications of spinal anesthesia is relieved when informed that he will recover eventually from his paralysis. This positive statement gains the proper cooperation from the patient for treatment and also can eliminate the possibly contemplated medicolegal action.

Spinal Muscular Atrophy.—Progressive spinal muscular atrophy has at times simulated spinal anesthesia complications. This condition in patients in whom the manifestations become gradually apparent, especially in the lower extremities, can simulate a lumbar herniated disk, as shown by Shea and co-workers in 1950.[15] A few of these patients have undergone laminectomy under spinal anesthesia. The subsequent progressive muscular wasting of both lower extremities has imitated the complications of spinal anesthesia. This disease not only simulates cauda equina radiculopathy but, as it progresses, also involves the upper extremities. The resulting clinical picture imitates chronic adhesive arachnoiditis. Although the clinical manifestations may be limited to the lower extremities, the electromyographic changes are plurisegmental in distribution and are accompanied by pathological fasciculations. The changes are detected immediately. The distribution of the denervation and the time it is detected differentiates this disease from cauda equina radiculopathy, in which the changes are restricted and will not be detected until three weeks after the spinal anesthesia. Here we have a specific example which illustrates the importance of immediate electromyographic evaluation—as soon as the muscular weakness manifests itself.

Myopathy and Myotonia.—At times, the myopathies and myotonia may simulate complications of spinal anesthesia. Some patients suffering from the distal form of muscular dystrophy, as well as some with myotonia, have claimed that the atrophy and/or muscle spasms were noted after spinal anesthesia. The differential diagnosis is a matter of great simplicity. First of all, no denervation activity is found, but dystrophic and/or myotonic activity are recorded. These findings rule out complications of spinal anesthesia.

Multiple Sclerosis.—Recurrent attacks of multiple sclerosis at times have taken place during the period of spinal anesthesia. The muscular deficit produced by this disease has been thought to be the result of the anesthetic agent. Multiple sclerosis, being an upper motor neuron disease, gives no electromyographic changes. Therefore, spinal anesthesia complications are definitely ruled out.

Disuse Atrophy.—Disuse atrophy, as reported by one of us and Rand in 1958,[16] is the result of lack of use of the voluntary muscles; it has been observed to occur in numerous conditions, especially in hysteria and in bone pathology or upper motor neuron lesions. Again, on occasion, spinal anesthesia has been erroneously incriminated. In these cases, the electromyographic findings are absolutely normal.

Hysteria.—Conversion hysteria, manifested in the form of paralysis of one or both lower extremities, also has imitated complications after spinal anesthesia.

Electromyogram in Differential Diagnosis

In the past few years, the electromyogram has been used by one of us (A. A. M.) to evaluate a large series of patients suffering from muscular weakness or paralysis as caused by a number of neurological conditions. The manifestations were not infrequently alleged to stem from spinal anesthesia. In a large series of cases, this allegation was worthy of critical analysis in 482. With the aid of the electromyogram, the true nature of the situation was unmasked. It is noteworthy that there was evidence of true complications of spinal anesthesia in only 4 patients, while in the remaining 478 the condition was actually due to an unrelated disease. Because the electromyogram plays a fundamental role in the evaluation of these complications, it is only proper that a brief basic résumé of clinical electromyography should be presented.

The present communication is concerned with the profound complications which follow spinal anesthesia and a group of other conditions which simulate it. Differentiation in these two groups of lesions

is based on two basic elements: (1) the distribution of the denervation, that is, electromyographic changes, and (2) the time in which the denervation activity is first detected electromyographically.

The precise location of the lesion can be determined by the distribution of the denervation and altered motor units. For example, in true complications of spinal anesthesia,[9] the denervation activity will not be detected until three weeks after the actual administration of the anesthetic agent. The distribution of the denervation activity is uniform and restricted. In a typical case of a true cauda equina radiculopathy, the changes will be found in the paraspinal muscles, the pelvic girdle, and the muscles of both lower extremities, that is, in the muscles innervated from about the level of L-1 down to the first coccygeal nerve root, in the lumbosacral plexuses, and in all the peripheral nerves of both lower extremities. No denervation activity will be found above the level of L-1, in the muscles of the cranial nerves, in the cervical or thoracic nerve roots, or in the peripheral nerves of the upper extremities—arms, forearms, or hands. In short, the changes are uniform in distribution and restricted in area and will appear three weeks after the administration of the spinal anesthesia.

In patients in whom the complications eventually assume the clinical picture of chronic progressive adhesive spinal arachnoiditis,[2] the electromyographic changes will start to appear after the third postoperative week and they will be found in the nerve roots of the lumbosacral region, in the corresponding plexuses, and in the peripheral nerves of the lower extremities. As time goes on, the electromyographic changes gradually assume an ascending trend which finally involves the paraspinal muscles of the thoracic and cervical regions, as well as those of the upper extremities.

The electromyographic changes in virus neuronitis[12] are widespread, involving the paraspinal muscles as well as the extremities. As a rule, the denervation decreases on ascending from the extremities to the muscles of the back. In a typical case, one finds changes in both feet, legs, and thighs, in the pelvic girdle, and in the paraspinal muscles, with the changes in the paraspinal muscles fading out as one approaches the eighth dorsal level. Occasionally, changes are also found in the distal portion of both upper extremities and in the muscles of the face. In spite of uneven widespread electromyographic changes, the patient may complain of weakness or paralysis in the low part of the back and in one or both lower extremities simulating a true complication of a spinal anesthesia. In short, the changes are uneven in distribution and will be detected as soon as the apparent complications manifest themselves.

Patients suffering from acute infections polyneuritis show electromyographic changes in both extremities and no changes in the paraspinal muscles. Here again, the clinical manifestations may be limited in one or both lower extremities, simulating a cauda equina lesion. In short, the changes will be detected immediately and are essentially peripheral in distribution.

Electromyographic changes in involvement of the lumbosacral plexus will, of course, not be found in the paraspinal muscles. They will be present in the gluteal group, the thigh, and the muscles of the leg and foot. The main differential point consists in finding no changes in the paraspinal muscles.

In cases of involvement of the sacral plexus, changes will be present in the gluteal group, the hamstrings, and the muscles of the leg and foot. No changes will be found in the quadriceps or adductor group or in the paraspinal muscles, which rules out a diagnosis of complication of spinal anesthesia.

Lesions of the femoral nerve[17] show denervation activity only in the quadriceps, with none in the paraspinal muscles, which will differentiate such a lesion from the cauda equina in which denervation activity will be found uniformly in the paraspinal muscles as well as in both lower extremities.

A lesion affecting the obturator nerve will show changes confined in adductors. A lesion of the peroneal nerve shows changes only in the muscles innervated by the common peroneal nerve on the side of the leg.

Tibial nerve lesions at the level of the popliteal fossa may also simulate the true complications of spinal anesthesia. However, denervation activity in tibial nerve lesions is confined only in the muscles of the back of the leg and foot. None are found above the level of the knee.

Plantar nerve lesions[18] are now believed to be one of the most misleading of nerve lesions. This lesion has simulated lumbar herniated disk syndrome, for which some patients have had a laminectomy. The persistence or aggravation of the symptoms have been alleged to be the result of postanesthesia complications. The electromyographic changes are confined only in the intrinsic muscles of the involved foot instead of the distribution of the nerve root for which the patient had the surgery.[18]

To sum up, the differentiation between lesions of either the nerve plexuses or the individual peripheral nerves and the complications of spinal anesthesia is that in the complications denervation activity will be found in both the paraspinal muscles and those of the lower extremities while in disorders of the plexuses and of the peripheral nerves the electromyographic changes are confined to the re-

spective muscle groups. Furthermore, if the lesion involving the plexus or the peripheral nerves preexisted the spinal anesthesia for three weeks, the denervation activity will be detected as soon as the complications become apparent. On the other hand, if the lesion occurred during the period of surgery, the electromyographic changes will not be detected until three weeks after the surgery has been done. For this reason, the electromyogram should be done as soon as the complications manifest themselves.

In progressive spinal muscular atrophy, which may be confused with chronic adhesive arachnoiditis, the electromyographic changes will be present as soon as the complications manifest themselves and will be found to be widespread both in the paraspinal muscles and in all four extremities as well, even in the cranial nerves at times. Occasionally a distal form of progressive muscular dystrophy with physical alteration in the muscles of the leg can also simulate cauda equina radiculopathy. The electromyogram will show no denervation activity but, instead, dystrophic activity. Finally, the distal forms of myotonia have sometimes been confused with cauda equina radiculopathy because of the muscle spasms and muscle weakness of the lower extremities. The electromyogram, of course, will show no denervation activity but, rather, only myotonic activity.

Double Aspect of Spinal Anesthesia Complications

It is just as important to anticipate alleged complications of spinal anesthesia as it is to point out the true character of certain imitators of these complications. In other words, prevention of difficulty is just as worthwhile, perhaps even more so, as distinguishing between the true and false when neurological symptoms and signs appear after the anesthetic episode has occurred. The prophylactic aspects of the problem will be discussed first.

The prevention of misunderstanding about spinal anesthesia is so important that any reasonable steps in this direction are worthwhile. Because prodromata of many of the simulators of spinal complications can be suspected if not detected, the prospect for spinal anesthesia should be questioned about any episodes of recent upper respiratory infections, febrile states, vaccination, or the administration of antitoxins. The patient should be asked about the occurrence of neuropathic symptoms—radiating pains, especially in the thoracic, lumbar, or lumbosacral root zones, the presence of abnormal sensations in the form of numbness, tingling, or burning, and the impairment of loss of motor power. The excessive use of alcohol or of sedative drugs leading to stupor or lethargy should be investigated for complications complained of after the anesthesia has been given. An inquiry regarding symptoms suggestive of possible episodes of loss of consciousness, anterior poliomyelitis,[19] multiple sclerosis, progressive spinal muscular atrophy, or myopathy should also be investigated. In case of any doubt or suspicion, a neurological examination, lumbar puncture for possible changes, and, above all, an electromyogram to check on antecedent alteration is of vital importance in avoiding misinterpretation of postanesthesia complaints.

It is needless to urge the necessity of keeping accurate records of actual procedure, the verification of the agent used, the size of spinal needle, and the precise interspace at which the injection was done. A wise precaution in any case would be withdrawal of a few cubic centimeters of spinal fluid for cell count and total protein level before the spinal anesthesia is administered in case of any doubt, particularly because these tests can be done in a short time.

The second aspect of the problem deals with the postanesthesia manifestations which suggest complications. The first step is a consultation with a competent neurologist and the second an immediate and thorough electromyographic examination. The neurologist may bring to light evidence favoring some preanesthesia neurological disease or disorder which can account for the symptoms. He may also delineate a case of malingering or of conversion hysteria. The electromyogram may likewise help by demonstrating the preexistence of lower motor neuron disease, for, if significant changes are found, it may be assumed that such changes were due to a disease already existing at least three weeks prior to the administration of the anesthetic. Moreover, the electromyographic findings may indicate that the causative disorder is not in the anterior horn cells, the motor root, or peripheral nerves but in the muscles themselves. At times, this examination may show that the complication is incidental to the surgical procedure rather than the anesthetic. Spinal anesthesia can be incriminated only when characteristic root manifestations (cauda equina) are found in the lower spinal levels only after three weeks have elapsed. When there is any question as to complications, an electromyogram should be done or even repeated before the patient leaves the hospital. This is to rule out evidence of complications which may actually occur at home but later be charged to the spinal anesthesia. Such a repeat should be done about three weeks after the spinal was done, for, if no changes are present after that interval, the anesthetic agent can be exonerated.

Summary and Conclusions

Out of thousands of patients who have been given a spinal anesthetic only rarely does one develop a neurological complication. Nevertheless, the possibility of such a calamity has created among the laity an apprehension which manifests itself whenever this form of anesthesia is followed by any type of muscular weakness or paralysis. For this reason, it is not uncommon for some to assume that the spinal anesthetic is responsible for the development of any concurrent neurological manifestations. In the recent past, a large series of patients who alleged that muscular paralysis was a direct result of spinal anesthesia have been examined by the electromyogram.

As a basis for this study, 482 patients whose neurological complaints seemed to have some merit were critically investigated. It was rather surprising to learn that evidence of what seemed to be true complications of spinal anesthesia were found in only four patients of this group. In the remaining 478 patients the neurological complaints were due to some other concurrent and entirely unrelated conditions. These conditions had imitated actual complications of the spinal anesthetic agent. On this basis, it would appear that in only 1 of 120 cases (0.82%) did the paralysis actually prove to be due to a genuine anesthetic complication. This experience indicates that the true picture of such complications can be delineated only by competent neurological examination and a complete electromyographic study undertaken by an experienced electromyographer. This comprehensive evaluation of the picture should be undertaken just as soon as the muscular weakness or paralysis becomes apparent. This urgency is based on the observation that the damage to the spinal nerve roots due to the anesthetic agent will not manifest itself on the electromyogram until three weeks after the actual date of the anesthesia. Therefore, if one finds electromyographic changes immediately or soon after the spinal anesthesia, it presumes the preexistence of some other disorder. In the majority of instances, the causative disease proves to be either an infectious neuronitis or a peripheral neuropathy.

Thus, with the aid of the electromyogram it has been pointed out that often some other entirely unrelated condition is responsible for the apparent neurological complications of the spinal anesthesia. These conditions, actually counterfeits of postanesthesia complications, have falsely incriminated the anesthetic agent itself for the paralytic state in almost 99% of the cases examined. The anesthetic agent was actually responsible for the paralysis in about 1% of the patients examined.

1212 Shatto St. (17) (Dr. Marinacci).

References

1. Weddell, G.; Feinstein, B.; and Pattle, R. E.: Electrical Activity of Voluntary Muscle in Man Under Normal and Pathological Conditions, Brain **67**:178-257 (Sept.) 1944.

2. Marinacci, A. A.: Clinical Electromyography, Los Angeles, San Lucas Press, 1955.

3. Buchthal, F.: Introduction to Electromyography, Oslo, Norway, J. W. Cappelen, 1957.

4. Eaton, L. M., and Lambert, E. H.: Electromyography and Electric Stimulation of Nerves in Diseases of Motor Unit: Observations on Myasthenic Syndrome Associated with Malignant Tumors, J. A. M. A. **163**:1117-1124 (March 30) 1957.

5. Courville, C. B.: Untoward Effects of Spinal Anesthesia on Spinal Cord and Its Investments, Anesth. & Analg. **34**:313-333 (Nov.-Dec.) 1955.

6. Ferguson, F. R., and Watkins, K. H.: Paralysis of Bladder and Associated Neurological Sequelae of Spinal Anesthesia (Cauda Equina Syndrome), Brit. J. Surg. **23**:735-752 (April) 1938.

7. Thorsen, G.: Injuries due to Anesthetic Agent, Through Effect on Nervous Substance: Injuries Via Assumed Perineural Effect of Anesthetic Agent, Acta chir. scandinav. (supp. 121) **95**:146-212, 1947.

8. Kennedy, F.; Somberg, H. M.; and Goldberg, B. R.: Arachnoiditis and Paralysis Following Spinal Anesthesia, J. A. M. A. **129**:664-667 (Nov. 3) 1945. Reference 5.

9. Spielmeyer, W.: Veränderungen des Nervensystems nach Stovainanästhesie, München. med. Wchnschr. **55**:1629-1634 (Aug. 4) 1908.

10. Brock, S.; Bell, A.; and Davison, C.: Nervous Complications Following Spinal Anesthesia: Clinical Study of Seven Cases, with Tissue Study in One Instance, J. A. M. A. **108**:441-447 (Feb. 8) 1936.

11. Critchley, M., and others: Discussion on Neurological Sequelae of Spinal Anesthesia, Proc. Roy. Soc. Med. **30**:1007-1032 (June) 1937.

12. Marinacci, A. A., and Rand, C. W.: Electromyogram in Diagnosis of Infectious Neuronitis: With Particular Reference to Differential Diagnosis Between This Disease and Local Neurosurgical Lesions, Bull. Los Angeles Neurol. Soc. **21**:37-48 (March) 1956.

13. Marinacci, A. A.: Peripheral Nerve Complications in General Surgical Procedures: Value of Electromyography in Their Correct Evaluation, Bull. Los Angeles Neurol. Soc. **22**:20-27 (March) 1957.

14. Marinacci, A. A.: Paralysis of Legs in Sedentary Workers: Preliminary Report, Bull. Los Angeles Neurol. Soc. **22**:73-78 (June) 1957.

15. Shea, P. A.; Woods, W. W.; and Werden, D. H.: Electromyography in Diagnosis of Nerve Root Compression Syndrome, Arch. Neurol. & Psychiat. **64**:93-104 (July) 1950.

16. Marinacci, A. A., and Rand, C. W.: Nerve Lesions in Industry: Atrophy of Disuse as Confusing Element in Diagnosis: Value of Electromyography, California Med. **88**:33-38 (Jan.) 1958.

17. Marinacci, A. A.: Electromyogram in Femoral Nerve Lesions, Bull. Los Angeles Neurol. Soc. **21**:137-141 (Sept.) 1956.

18. Marinacci, A. A.: Clinical Manifestations of Plantar Nerve Disorders: Value of Electromyogram in Correct Evaluation of Lesion, Bull. Los Angeles Neurol. Soc. **22**:171-176 (Dec.) 1957.

19. Golseth, J. G., and Huddleston, O. L.: Electromyographic Diagnosis of Lower Motor Neuron Disease, Arch. Phys. Med. **30**:495-499 (Aug.) 1949.

CLINICAL NOTES

STAPHYLOCOCCIC ENDOCARDITIS TREATED WITH RISTOCETIN

Robert W. Weber, M.D., Kansas City, Kan.

The treatment of endocarditis caused by Staphylococcus (Micrococcus) pyogenes var. aureus has become a challenging problem; therefore, two patients successfully treated with a new antibiotic agent, ristocetin, are reported on here. In these two patients, the infections were acquired in hospitals and, as might be expected, the staphylococci were resistant to penicillin. Each was critically ill when therapy was started, and the use of ristocetin was associated with prompt clinical improvement and eventual bacteriological cure.

Thrombophlebitis of severe degree developed in both patients and complicated administration of the antibiotic, and severe leukopenia occurred approximately two weeks after the onset of therapy in both patients. These complications cleared after completion of therapy.

Report of Cases

Case 1.—A 32-year-old woman was admitted to the University of Kansas Medical Center on Oct. 9, 1957. She first noted the onset of chills and fever during the afternoon of Sept. 21. The next day, she was admitted to her local hospital and aborted a two-month-old fetus. The chills and fever continued and, two days later, a dilatation and curettage was performed. Initially, she was placed on therapy with penicillin and streptomycin, but she continued to have daily temperature elevations to between 104 and 105 F (40 and 40.5 C). She then received oxytetracycline, chlortetracycline, and novobiocin. During the 19 days in the local hospital, the patient was afebrile for only one six-hour period; this occurred after she was given corticotropin for four days prior to transfer to this hospital.

The history revealed numerous sore throats as a child, but no findings suggestive of rheumatic fever. There was no history of heart disease or of a heart murmur.

At the time of admission to this hospital, the patient complained of chills, fever, and weakness. She also described sharp pain, pleuritic in nature and present for two days, in the left anterior part of the chest.

Physical Examination.—The patient was an obese woman who was pale and appeared acutely and chronically ill. Blood pressure was 120/55 mm. Hg, pulse rate 120 per minute, respiratory rate 28 per minute, and temperature 101.6 F (38.6 C). Numerous hemangiomas were present over the anterior part of the chest and upper extremities. No petechiae were seen in the conjunctiva or elsewhere over the body. Rales were present in both lung bases and in the left anterior apical area of the lungs. The heart was enlarged to percussion. There was a gallop rhythm at the apex, and a grade 2 systolic murmur was present in the third interspace to the left of the sternum. The liver was palpable at the right costal margin. The spleen was not palpable. Pelvic examination was negative. Pitting edema of the ankles was demonstrated. Findings on neurological examination were within normal limits.

Laboratory Data.—Urinalysis showed a trace of albumin and microscopically many red blood cells and 8 to 16 pus cells per high-power field. The hemoglobin level was 8.7 Gm. per 100 ml., and the white blood cell count was 10,300 per cubic millimeter with 83% neutrophils. Results of serologic testing were negative. The blood urea nitrogen level was 15 mg. per 100 ml., and the blood sugar level was 84 mg. per 100 ml. The sedimentation rate was 33 minutes per hour (Cutler). The C-reactive protein precipitation was 4+, and the antistreptolysin-O titer was 333 units.

The electrocardiogram revealed a P-R interval of 0.16 second, and there was sinus tachycardia with 120 beats per minute. An infiltration was present in the left upper lung field on the roentgenogram, which was characteristic of a pulmonary infarction. The heart size was at the upper limits of normal.

During the first 12 hours after admission, eight blood cultures were obtained. A coagulase-positive, hemolytic Staph. pyogenes var. aureus was grown from each of these cultures, and, quantitatively, 45 to 248 colonies were isolated from each cubic centimeter of blood. The disk type of sensitivity study revealed only moderate sensitivity to erythromycin, chloramphenicol, and nitrofurantoin (Furadantin). Tube dilution sensitivities[1] are recorded in the table.

Tube Dilution Sensitivities, in Micrograms per Cubic Centimeter, in Two Patients Being Treated for Staphylococcic Endocarditis

Antibiotic	Case 1		Case 2	
	Sensitive to	Resistant to	Sensitive to	Resistant to
Erythromycin	0.16	0.08	0.08	**0.04**
Oleandomycin	0.50	0.25	...	...
Nitrofurantoin	37.50	20.00	...	...
Novobiocin	125.00	100.00	0.30	0.016
Penicillin (units)	1,000.00	500.00	62.50	50.00
Ristocetin	5.00	3.90	3.10	2.50
Chlortetracycline	...	...	0.60	0.30
Streptomycin	...	...	25.00	31.30

Hospital Course.—During the first 24 hours after admission, the patient was digitalized. Her temperature rose to 103.2 F (39.5 C) on Oct. 9 and to 104.6 F (40.3 C) the next day. She complained of pleuritic pain in the left anterior part of the chest, and a friction rub was audible in this area. On Oct. 10, after the eighth blood culture was obtained, novobiocin therapy was started. On Oct. 12, tube dilution sensitivities were available, and that therapy was discontinued. Erythromycin, 2 Gm. every six hours, was then given orally. The temperature curve is shown in fig. 1. Although she became afebrile after receiving erythromycin two days, the fever returned in five days and, clinically, she remained critically ill. Blood cultures were repeatedly negative after erythromycin therapy was begun. On Oct. 25, she complained of severe nausea and vomited after every meal. This continued until Oct. 27, when the erythromycin dosage was decreased to 1 Gm. every six hours. At this time, ristocetin therapy was begun. A "cut-down" (venostomy) on the

From the Department of Medicine and Microbiology, University of Kansas School of Medicine.

left small saphenous vein was performed and a polyethylene catheter inserted. Ristocetin, 1.5 Gm., was given intravenously in 500 cc. of 5% glucose in water every eight hours. This was administered in two hours and was followed by isotonic sodium chloride solution or 5% glucose in water given slowly, to maintain the cut-down. Twenty-four hours after starting the ristocetin therapy, the temperature returned to normal. On Nov. 4, the ristocetin dosage was decreased to 1 Gm. every 12 hours, and, on Nov. 8, this therapy was discontinued. The total dose was 44 Gm. Serum concentrations of ristocetin were determined four hours after administration of the antibiotic on four occasions. The levels on Oct. 30, Nov. 1, and Nov. 4 were 80 mcg. per cubic centimeter and on Nov. 7, 40 mcg.

On Oct. 29, thrombophlebitis developed in the left leg and a second cut-down was performed on the right leg. Severe thrombophlebitis also developed in this leg before therapy was discontinued. On Nov. 6, anticoagulant therapy with aqueous heparin and bishydroxycoumarin (Dicumarol) was begun. The thrombophlebitis improved after the institution of this therapy.

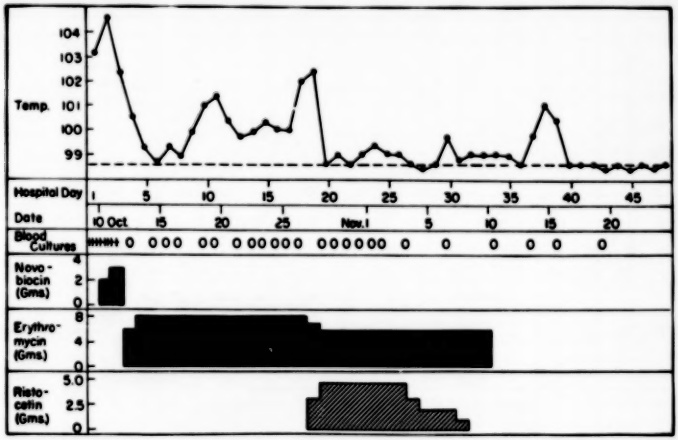


Fig. 1 (case 1).—Temperature curve of patient with staphylococcic endocarditis treated with novobiocin, erythromycin, and ristocetin.

As noted in figure 2, the white blood cell count was 3,700 per cubic millimeter, with 71% neutrophils, on Nov. 8, when the ristocetin therapy was discontinued. During the next seven days, the count declined to 1,400, with 4% neutrophils. The eosinophil count did not rise until the white blood cell count and neutrophils increased in number. Specific therapy was not instituted for the neutropenia, and antibiotics were not administered during this period. The hemoglobin level and platelet counts remained unchanged.

After the thrombophlebitis subsided, the patient became afebrile and asymptomatic. The heart murmur was heard with difficulty when she was dismissed from the hospital. Correspondence with her local physician two months after her discharge revealed that the patient had resumed her duties as a housewife.

The origin of the staphylococcic bacteremia in this patient is difficult to establish, and several possibilities exist. Three of her children had recently been hospitalized with sore throats, and a staphylococcic infection may have been acquired from them prior to her hospital admission. Infection may have occurred in the hospital after the abortion and subsequent curettage. Sensitivity studies on the organism which was isolated from the blood cultures would suggest that this was a hospital strain of staphylococcus.

Location of the heart murmur in the second left intercostal interspace and absence of transmission of this murmur into the neck would indicate the pulmonary valve as the site of the endocarditis. Pulmonary embolization, in the absence of demonstrable disease in the peripheral veins, would substantiate this impression. Further evidence was the changing heart murmur after therapy. A murmur had not been described previously, although the patient had been examined repeatedly during six previous pregnancies.

Resistance of this staphylococcus to novobiocin was unusual, but the antibiotic had been administered in inadequate amounts, 750 mg. daily for one week, before sensitivity studies were made. Rantz and co-workers [2] reported a similar experience in a young woman with staphylococcic endocarditis. Their patient received 1 Gm. of novobiocin daily for three days, and, when sensitivity studies were performed later, the organism had increased its resistance to this antibiotic from 0.5 mcg. to 20 mcg. per cubic centimeter. Unfortunately, previous cultures were not obtained in this patient, but it is likely that the resistance developed while she was

receiving the antibiotic in relatively small amounts. Novobiocin was given here for only two days and did not affect the clinical course.

Initially, the response to erythromycin was encouraging, but, after five days, clinical deterioration began and fever returned. Previous reports of the ineffectiveness of erythromycin alone in the treatment of staphylococcic endocarditis further emphasized the necessity of use of a second antibiotic agent.[3] Sensitivity studies indicated that ristocetin would be effective, and adequate serum levels were demonstrated after its administration.

CASE 2.—A 21-year-old woman was admitted to the University of Kansas Medical Center on Oct. 7, 1957. She complained of weakness and painful swelling of the joints and muscles.

She was first hospitalized at another hospital, Aug. 19, 1957, because of dysmenorrhea. A laparotomy was performed on Aug. 21, and a corpus luteum cyst was removed. Excessive uterine bleeding occurred after surgery, and curettage was performed on the sixth postoperative day. She became febrile after this procedure and was given penicillin, streptomycin, sulfadiazine, and tetracycline. On Sept. 1, she complained of generalized muscular aching and joint pains. On Sept. 12, an abscess was noted in the left antecubital fossa, and, on Sept. 20, a second abscess was noted in the right antecubital area. The temperature was frequently elevated to 102 to 103 F (38.8 to 39.4 C), and arthralgia and myalgia increased. A muscle biopsy was obtained, and a diagnosis of dermatomyositis was suggested. Corticotropin and cortisone therapy was started on Sept. 27. Although the fever subsided with steroid therapy, other symptoms remained and she was transferred to this hospital while still receiving antibiotic therapy.

Her history revealed that a diagnosis of acute rheumatic fever had been made in 1954. She described joint pains and fever with this illness. A heart murmur was also discovered at this time. The symptoms disappeared without treatment or bed rest. In 1947, she had pneumonia and, in 1951, an appendectomy. During the previous years in college, she had had numerous respiratory infections characterized by cough and rhinitis.

Physical Examination.—The patient was pale and appeared chronically ill but was in no acute distress. She weighed 125 lb. (58.5 kg.). Blood pressure was 110/60 mm. Hg and pulse rate was 72 per minute and regular. A grade 2, blowing, systolic murmur was heard in the third intercostal interspace, immediately to the left of the sternum, and was transmitted over the base of the heart and into the carotid arteries. A recent, well-healed, suprapubic scar was present. The liver and spleen were not palpable. Minimal pitting edema was present in both lower extremities. The bilateral anticubital abscesses were healing, and pus could not be extracted on pressure.

Laboratory Data.—Urinalysis revealed a heavy trace of albumin, occasional pus, and occasional red blood cells. The hemoglobin level was 12.8 Gm. per 100 ml., and the white blood cell count was 16,000 per cubic millimeter, with 73% neutrophils, 21% lymphocytes, 3% monocytes, and 1% eosinophils. Findings on the Venereal Disease Research Laboratory test were negative. L.E. cells were not observed in peripheral blood. The agglutination test for heterophil antibodies was positive in a 1:14 dilution. The sedimentation rate was 15 mm. per hour. The antistreptolysin-O titer was 12 units. Findings on the electrocardiogram were within normal limits. A normal-sized heart and clear lung fields were seen on x-ray examination. Six blood cultures were obtained, and no growth was observed aerobically or anaerobically.

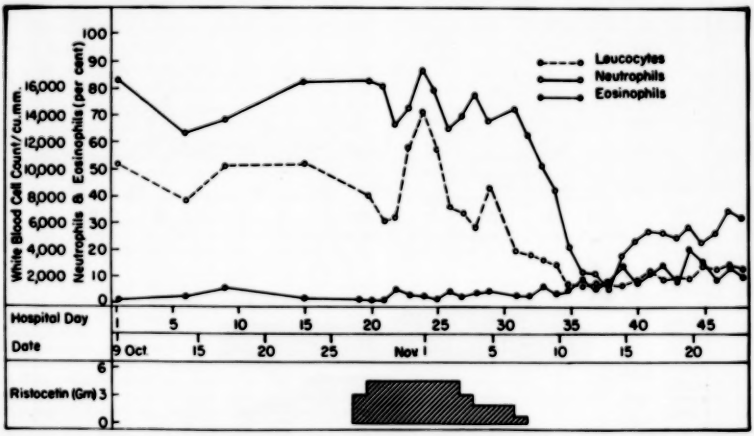


Fig. 2 (case 1).—Effect of ristocetin on leukocyte, neutrophil, and eosinophil counts in patient with staphylococcic endocarditis.

Hospital Course.—During the next 10 days in the hospital, the maximum daily temperature was between 99.4 and 101 F (37.4 and 38.3 C). The dosage of cortisone was gradually decreased, and therapy with this drug was discontinued on the ninth day. Therapy with antibiotics was discontinued on admission. The patient continued to complain of muscle aching, but no objective findings were observed.

On Oct. 17,1957, the patient was allowed to go home for four days. On Oct. 21 she returned to the hospital with chills and fever. The temperature was 104 F (40 C). The physical findings were essentially unchanged, and no petechiae were noted. The initial blood culture grew 183 colonies of hemolytic Staph. pyogenes var. aureus, coagulase-positive, per cubic centimeter of blood. Four blood cultures were obtained during the first 12 hours in the hospital, and all were positive.

Therapy with aqueous sodium penicillin G, 5 million units every six hours, was started on Oct. 22, before sensitivity studies were available. Novobiocin, 1 Gm. every six hours, was given the following day on the basis of disk sensitivity study results. A novobiocin blood level of 38.4 mcg. per cubic centimeter of serum was obtained 24 hours after starting therapy with this antibiotic. The tube dilution sensitivity results are recorded in the table.

Novobiocin therapy was continued until Oct. 27, as noted in figure 3, when it was discontinued because the patient developed a generalized erythematous macular rash. Nausea and vomiting also occurred frequently after this medicament was given. On Oct. 26, petechiae were first noted on the abdomen. Therapy with erythromycin, 1 Gm. orally every eight hours, and ristocetin, 1 Gm. intravenously every six hours in 500 cc. of 5% glucose in water, was begun when that with novobiocin was discontinued. It was necessary to insert a polyethylene catheter into the small saphenous vein to give the intravenous therapy. Within two days, thrombophlebitis developed in this leg, but therapy with ristocetin was continued because, clinically, the patient was improving. Bishydroxycoumarin therapy was started on Nov. 2. The pain and swelling increased, and, on Nov. 5, a cut-down was performed on the right leg. On Nov. 3, the ristocetin dosage was decreased to 2 Gm. daily, and therapy with this drug was discontinued on Nov. 11. The right leg also became acutely tender along the saphenous vein, and marked swelling occurred. The thrombophlebitis subsided slowly, and the patient remained febrile until it resolved. Erythromycin therapy was continued until Nov. 27, but it had no apparent effect on the temperature course.

A total of 42 Gm. of ristocetin was given to this patient. Serum concentrations of this antibiotic were determined on four occasions, four hours after administration of the drug. Staphylococci previously isolated from this patient, with known sensitivity to ristocetin, were used in determining the serum concentrations. Serial dilutions of the serum were tested to inhibit growth of this organism. The ristocetin serum levels were 793.6 mcg. per cubic centimeter on Oct. 30, 198.4 mcg on Nov. 1, 49.6 mcg. on Nov. 4, and 396.8 mcg. on Nov. 7.

The white blood cell counts are shown in figure 4. On Nov. 11, she received a single injection of 80 units of ACTH gel intramuscularly. She received no medicaments except erythromycin after this. Hemoglobin level and platelet count, determined daily, remained unchanged from normal.

The systolic heart murmur decreased to grade 2 in intensity. After her discharge from the hospital, she was examined on Dec. 20, 1957, and Jan. 15 and Feb. 4, 1958. Fever and symptoms did not return, and she began working regularly as a medical technician on Jan. 15. On this date, the sedimentation rate was 10 mm. per hour and the white blood cell count was 13,320 per cubic millimeter, with 67% neutrophils.

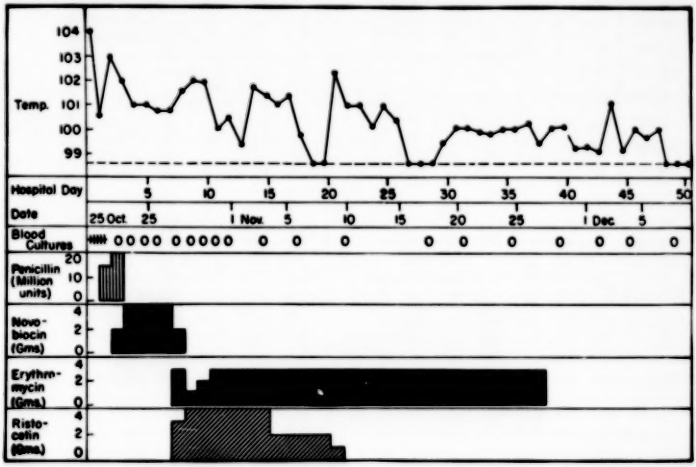


Fig. 3 (case 2).—Temperature curve of patient with staphylococcic endocarditis treated with penicillin, novobiocin, erythromycin, and ristocetin.

The previous administration of various antibiotics and steroids initially confused the clinical picture, interfering with establishment of the correct diagnosis. Dermatomyositis was considered, but the absence of physical findings and the subsequent clinical course did not support this diagnosis.

The staphylococcic infection in this patient may have originated from various sources, but at least a "hospital organism" seems involved. Prior to her operation, she had been employed as a medical technician in a large general hospital and could have acquired colonization with hospital strains of staphylococci. The abscesses which developed in the antecubital fossa most likely indicate the site

and the source of the staphylococcic bacteremia which resulted in the endocarditis. The history of probable rheumatic fever suggests that the infection occurred on a previously diseased heart valve. A changing aortic systolic murmur and the peripheral emboli would further indicate the aortic valve to be the site of the endocarditis.

Novobiocin had not been administered to this patient previously. Sensitivity studies suggested that this antibiotic could be given in effective amounts. The erythematous rash, fever, and nausea and vomiting which occurred after four days forced discontinuance of this antibiotic. Because of the experience in the previous patient with administration of erythromycin alone, therapy with both erythromycin and ristocetin was started simultaneously. The patient was acutely ill at this time and had numerous petechiae. The clinical improvement which followed warranted the continuation of ristocetin therapy despite the appearance of severe phlebitis in the injected veins.

The persistence of fever despite negative blood cultures was quite disturbing. Clinically, the patient improved dramatically, and laboratory tests substantiated this observation. Fever probably resulted from a combination of the leukopenia and severe bilateral thrombophlebitis. After these improved, she became and has remained afebrile.

Comment

The problem of hospital-acquired staphylococcic infections is well recognized, and the necessity for new antibiotic agents in the treatment of these infections is unquestioned. It would also be desirable that such an antibiotic be reserved for use only in the more serious staphylococcic infections. Ristocetin, therefore, seems to be ideal in meeting this need. The necessity for intravenous administration, the occurrence of thrombophlebitis, and the accompanying striking leukopenia should assure the infrequency of its use in treating less serious infections.

Leukopenia and neutropenia have been reported after the use of ristocetin.[4] Eosinophilia occurring before the leukopenia appears has also been described, but, in these two patients, eosinophilia did not appear until the patients were recovering from their leukopenia. It should be noted that the leukopenia occurred in both instances 15 days after starting therapy with this antibiotic and two days after it had been discontinued. Hemoglobin levels and platelet counts remained essentially unchanged from the values noted before steroid or other therapy was instituted.

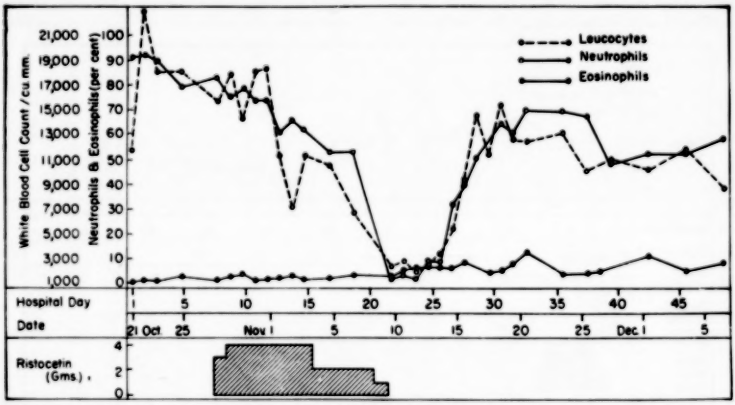


Fig. 4 (case 2).—Effect of ristocetin on leukocyte, neutrophil, and eosinophil counts in patient with stapylococcic endocarditis.

Summary

In two cases of hospital-acquired staphylococcic bacterial endocarditis the patients were treated with ristocetin and erythromycin, with clinical and bacteriological cures. Severe leukopenia and neutropenia occurred in both patients after the use of 44 and 42 Gm., respectively, of ristocetin in 13 days. The hemoglobin levels and platelet counts remained normal. The white blood cell counts gradually returned to normal limits.

Thrombophlebitis also developed in both patients during the intravenous administration of the antibiotic. The thrombophlebitis was severe and was responsible for persistence of fever in one of

the patients. Ristocetin is a valuable antibiotic in the treatment of serious hospital-acquired staphylococcic infections.

Kathryn Rodecker, M.A., performed the bacteriological studies.

The ristocetin used in this study was supplied as Spontin by Abbott Laboratories, North Chicago, Ill.

References

1. Grove, D. C., and Randall, W. A.: Assay Methods of Antibiotics: Laboratory Manual, New York, Medical Encyclopedia, Inc., 1955, p. 238.

2. Rantz, L. A.; Randall, E.; Thum, L.; and Barker, L. F.: Effects of Vancomycin, Oleandomycin, and Novobiocin on Staphylococci in Vitro, Antibiotics & Chemother. **7**:399-409 (Aug.) 1957.

3. Finland, M.: Staphylococci, Antibiotics, and Endocarditis, editorial, Circulation **15**:641-645 (May) 1957. Geraci, J. E., and Martin, W. J.: Antibiotic Therapy of Bacterial Endocarditis: V. Therapeutic Considerations of Erythromycin, Proc. Staff Meet. Mayo Clin. **29**:109-118 (Feb. 24) 1954. Haight, T. H., and Finland, M.: Resistance of Bacteria to Erythromycin, Proc. Soc. Exper. Biol. & Med. **81**:183-188 (Oct.) 1952. Roantree, R. J., and Rantz, L. A.: Fatal Staphylococcal Endocarditis Treated with Erythromycin: Rapid Development of Resistance in Vivo and in Vitra, A. M. A. Arch. Int. Med. **95**:320-325 (Feb.) 1955.

4. Romansky, M. J.; Limson, B. M.; and Hawkins, J. E.: Ristocetin: New Antibiotic—Laboratory and Clinical Studies, Preliminary Report, in Antibiotics Annual, 1956-1957, edited by H. Welch and F. Marti-Ibañez, New York, Medical Encyclopedia, Inc., 1957, pp. 706-715. Newton, R. M., and Ward, V. G.: Leukopenia Associated with Histocetin (Spontin) Administration, J. A. M. A. **166**:1956-1959 (April 19) 1958. Gangarosa, E. J.; Landerman, N. S.; Rosch, P. J.; and Herndon, E. G., Jr.: Hematologic Complications Arising During Ristocetin Therapy: Relation Between Dose and Toxicity, New England J. Med. **259**:156-161 (July 24) 1958.

COUNCIL ON INDUSTRIAL HEALTH

SOME MEDICOLEGAL ASPECTS OF OCCUPATIONAL DERMATOSES

This is the fourth in a series of reports prepared by the Committee on Occupational Dermatoses of the Council on Industrial Health, American Medical Association.

B. Dixon Holland, M.D., *Secretary.*

Despite the fact that remarkable strides have been made in preventive medicine and that with few exceptions occupational diseases are preventable, thousands of occupational dermatoses claims are compensated each year. Differentiating industrial skin diseases from clinically similar skin disorders occurring in ordinary life is a major problem in itself. Even more troublesome to the physician are problems arising from the medicolegal aspects of compensation. In all likelihood, these difficulties will continue to grow rather than decline, particularly in view of the increasingly complex number of contact agents being handled in industry. The American Medical Association Committee on Occupational Dermatoses, therefore, considers it timely to review some medicolegal aspects encountered in occupational dermatology. Although most physicians have had to deal with compensation matters, there still remains a great need for educating the profession in this field.

The first workmen's compensation law in the United States was passed in 1908 by the federal government for the benefit of certain civil employees, and in the states in 1911. The early laws afforded no specific coverage for occupational diseases. At the present time, all states compensate for occupational accidents and all but two states provide for total or limited coverage of occupational disease. Eighteen states and Puerto Rico have schedule laws which cover only listed diseases, while the rest of the jurisdictions provide for full coverage.[1] Under full coverage laws industrial dermatitis is subject to the same compensation provisions as other occupational diseases. However, laws with schedule coverage of occupational diseases tend to limit the types of industrial skin diseases considered compensable or define the agents which must produce the disease.

The object of workmen's compensation is to assure payment to the worker for wages lost and certain related medical costs because of injury or illness incurred on the job, regardless of who is at fault, and to rehabilitate the patient as well as possible. The compensation laws vary considerably from state to state in scope, coverage, and benefits. Likewise, there is a lack of uniformity in the interpretation and application of such laws. This lack of uniformity creates many problems in the litigation of an injury and illness including dermatitis incurred from work.

Among the many legal definitions for an occupational disease is: "An occupational disease is one peculiar to the occupation in which the employee was engaged and due to causes in excess of ordinary hazards of employment as such."[2] Sappington[3] has defined an occupational disease as "one which

The members of the Committee on Occupational Dermatoses are Drs. Donald J. Birmingham (Chairman), Cincinnati; Leonard Weber (Secretary), Chicago; Frank C. Combes, New York; A. Fletcher Hall, Santa Monica, Calif.; James W. Jordan, Buffalo; George Morris, Boston; and Ray O. Noojin, Birmingham, Ala.

occurs with characteristic frequency and regularity in occupations where there is a specific hazard as the cause which operates to produce effects in the human body recognized clinically by the medical profession as pathologic changes and effects produced by the specific occupational hazard involved."

An occupational dermatitis has been defined as an inflammatory condition of the skin incidental to one's occupation. Broadly, this definition would include the housewife's dermatitis, the gardener's plant poisoning of the skin, and the architect's dermatitis from his teakwood ruler. Actually, an occupational dermatosis is any abnormality or pathological condition of the skin due to occupation. These definitions seem fairly simple, but the industrial physician, even the dermatologist, may have difficulty in determining whether or not the cause for a given cutaneous eruption is of industrial nature.[4]

It is important that the practicing physician familiarize himself with the compensation law in his own state as well as with the peculiarities associated with particular compensation problems in occupational dermatoses. For these reasons, we have deliberately chosen to elaborate on certain topics of current interest in order to emphasize their relationship to legal aspects of an occupational skin disease.

Sensitivity

An interesting problem is presented by the employee who, by reason of his occupation, has developed a specific sensitivity to a certain substance which makes him unfit to continue his trade, although his condition is not such as to disable him physically. In one case,[5] the claimant had been disabled by a dermatitis from September, 1932, until April 12, 1933, when he returned to his occupation. On June 14, 1933, he was told that he could work no longer on account of his sensitivity. He then was awarded total disability by the industrial accident board. The court decided that, although the original eruption had disappeared, the employee's skin had never returned to normal; testimony in the record was sufficient to justify a finding of "disability as to the particular employment, but not as to employment in general. It was the duty of the employee to try to get other work."

Claims for permanent disability from sensitization are now plaguing the courts. One such set of claims due to sensitization from chrome compounds among railroad workers employed in the maintenance of diesel engines is of interest at the present time.

Another case [6] is reported in which a claimant sought a compensation award for permanent disability resulting from his sensitivity to cinnamon. From a denial of such award the claimant appealed to the U. S. District Court of Appeals, first district, division 1, California. He had worked as a baker since 1922, handling cinnamon without harmful results. In November, 1948, he was employed as a pastry baker. The following February a rash developed on his hands, becoming so acute that he quit work on March 10, 1949. The commission determined that he had contracted a disabling dermatitis which was caused by sensitivity to cinnamon and gave him temporary total compensation.

The condition disappeared in April, and he went to work as a baker for another employer. After three days the condition reappeared, and a few days later he was again forced to quit work. After a short period of rest the condition disappeared. Twice later he went to work for other employers and after extremely short periods of employment again broke out with a dermatitis due to his sensitivity to contact with cinnamon. Each time he received total compensation, each time his dermatitis cleared on cessation of contact with cinnamon, and reappeared on subsequent exposure. He then filed his petition for a permanent disability rating. At the hearing before the commissioner the claimant submitted the reports of five physicians, one of whom was his personal physician. All agreed substantially that at that time he was sensitive to cinnamon and that his exposure to it produced a dermatitis. None of the physicians other than his own reported on the permanency of this sensitivity. The only medical evidence in the record is the following report of his personal physician: "Because this skin test is still positive to cinnamon, the patient would still be unable to work as a baker without having a recurrence of his skin eruption as long as he contacts cinnamon. This skin sensitivity to cinnamon will probably remain for an indefinite period of time, but it is impossible to know how long such a sensitivity will remain."

On the basis of this evidence the claimant then contended on appeal that the commissioner erred in finding that the claimant suffered no permanent disability. After pointing out that whether the injury was permanent at a particular time was purely a question of fact and that the burden of proof was on the claimant to show that his sensitivity to cinnamon was permanent, the court of appeals said that it was a fact that on four different occasions since 1949, when exposed to cinnamon, dermatitis developed, and all the physicians agreed that the claimant is now sensitive to cinnamon, and exposure to it at present will result in dermatitis. These facts alone, continued the court, do not establish that such condition will continue for the balance of his life or meet the test of permanent disability. A disability is generally regarded as permanent when further change, for better or worse, is not to be reasonably anticipated under usual medical standards. The court of appeals affirmed the denial of an award by the compensation commissioner.

In another case,[7] the workman, about 41 years of age, was employed from 1935 to August, 1940, in the gasoline and petroleum products bulk station of the defendant corporation unloading gasoline from tank cars and loading gasoline into trucks. Sometime after entering his employment he developed a dermatitis which did not result in disability. In the summer of 1939 an eruption developed on his hands, arms, and face; it was diagnosed by a dermatologist as an allergic dermatitis due to contact with gasoline and he was treated at intervals for about two months. On April 27, 1940, he again developed an eruption on his hands, and was again treated until June 22, 1940, when the eruption was pronounced as cured. He continued at his regular work until Aug. 31, 1940, when the employment was terminated by the employer because the workman "was allergic to gasoline poison." He instituted proceedings under the workman's occupational disease act of Indiana for compensation, "alleging that in the performance of the duties of his employment . . . he was exposed to an occupational disease and that he is afflicted therefrom with 'gasoline poisoning-dermatitis-due to gasoline poisoning.'" The industrial board found that the workman contracted an occupational disease by reason of his employment, that he was totally disabled from that disease on Aug. 31, 1940, the date his employment was terminated by the employer, and that he was totally disabled from that date until the hearing before the board, some four months later. An award of compensation was made accordingly in his favor, and the employer appealed to the appellate court of Indiana. Applying the facts in the case, the court concluded that the finding and award of the industrial board was erroneous. The workman was not disabled on the 31st day of August, 1940. When his employment was terminated on the latter date he suffered no disability that caused any loss of time or wages or that would entitle him to be designated as disabled under the act. "It is possible that the allergy still exists, but a fair interpretation of the act leads us to the conclusion that a mere allergic condition from which some affliction might develop was not contemplated in the act." The award in favor of the workman was accordingly reversed.

In another case [8] occupational dermatitis was considered an accident. A workman in New Mexico instituted suit under the workmen's compensation act against his employer and the employer's insurer for an injury alleged to have been accidental and to have arisen out of and in the course of his employment as a printer. The trial courts found that in the course of his employment it was necessary that he cleanse his hands frequently with a soap furnished by the employer. The court found that the use of the soap would not have caused injury to the workman except for his allergy and that the resulting injuries constituted an unlooked for mishap which was neither expected nor designed and which was accidentally caused. Accordingly compensation was awarded the workman, and the employer and the insurer appealed to the Supreme Court of New Mexico. The employer and insurer denied that the disability suffered by the workman was accidental because, so they contended, the so-called injury was not related to any specific time or event, a necessary fact to be found, so they asserted, to support a judgment in his favor. The New Mexico statutes, answered the Supreme Court, not only do not define the word accident but do not undertake to limit its meaning to "sudden" injuries as do those of a number of the states, nor is its meaning limited by any time test. Accidental injuries, continued the court, are usually sudden happenings; and the time, event, and circumstances can be definitely determined, but there are exceptional cases in which injuries are unquestionably accidental, although the precise time of their beginning is uncertain, such as those caused by breathing dust or gases, frost bite, slow poisoning, or a series of slight injuries culminating in a serious one. An injury may be gradual and progressive, and not immediately discoverable, yet certainly and definitely progress to discovery and then to compensable injury. Such was the injury to the workman in this case. The time did arrive when his injuries totally disabled him so he could not work, and at that time he became entitled to compensation for total disability. The washing of the workman's hands was a necessary part of the labor for which he was employed. His injury, therefore, arose out of and was suffered in the course of his employment, and, if accidental, it was compensable. It comes under the classification: an injury that was the unintended result of an intentional act; received while performing his labor under the usual and ordinary conditions of his employment. The plant soap was a poison to the workman, and his injury was compensable. The judgment of the trial court in favor of the workman was accordingly affirmed.

New Injury or Recurrence

In Massachusetts the board has certain fixed ideas regarding medical aspects of occupational dermatoses. Conspicuous among these are the words "new injuries" and "recurrences." If a man suffers a disability from an injury caused by an industrial dermatitis, he is entitled to compensation. If this dermatitis is relieved so that there are no clinical evidences of it remaining, and the man returns to work, any subsequent outbreak due to further exposure is a new injury and the liability should be assumed by the insurer of the last concern by whom he was employed. If, however, the worker returned to work while the original dermatitis was still present and as a result of this work he has an acute exacerbation of his previous dermatitis, then the company who insured the original employer is liable for compensation for disability resulting from this

later renewed activity of the occupational dermatitis. It is on these apparent primary facts that many hearings are held at the industrial accident board and as many as three or more insurers may be involved in one case.

Appeals must come to the superior or supreme courts on questions of law and not on questions of fact. Legal representatives of employers and employees go to considerable expense and trouble in an effort to establish definite rules of law for general guidance in the handling of workmen's compensation cases. As a result of decisions made the industrial accident board has tried to adhere to the rule that once an employee is relieved, that is, shows no clinical evidence of his dermatitis and returns to work, any subsequent outbreak is a new injury for which the liability rests on the insurer of the employer at the time of the second attack, whether or not he is the original insurer.[9]

There were, however, three decrees of the State Supreme Court of Massachusetts concerning cases in which the employees, after having received compensation from the insurers of their employers, went to work for other employers where they were subjected to irritants and became disabled again, and where the industrial accident board had held the original insurers liable for the compensation. The Supreme Court reversed these decisions and said that in each case there was no evidence that the subsequent attacks of dermatitis were due to the original exposure rather than the later contact with irritants, the latter being an independent intervening cause which broke the chain of causation between what happened originally and the disability in question.[10] A fourth case contained evidence of a conflicting nature; upon practically every point again the board held the original insurer liable. This time the court sustained the board and decided that the evidence warranted a finding that the original dermatitis never cleared up and that, since there was no evidence to show that the further exposures affected the original condition, the rule laid in the previous cases was not applicable.[11]

Inasmuch as the annual workmen's compensation insurance premiums of an employer are influenced by the amount of money paid as benefits under the act, there is an incentive for concerns to throw back the liability onto a previous insurer. As opinions of the physicians and resulting decisions must depend almost entirely on the statements of the claimant and others, it is here that we often listen to testimony of apparently prejudiced witnesses. When we ask a private patient, not seeking compensation or redress for his dermatitis or eczema, the duration of his eruption he may unhesitatingly say "years." However, careful analysis reveals that it may be periodic or may have cleared at various times only to reappear days, weeks, or months later. So the employee seeking compensation may truthfully state his eruption has been present since the original onset. He may believe he has been poisoned, and it is in his system; hence, the value of a careful history, and also the supreme necessity of treating a patient until every vestige of the dermatitis has disappeared for a reasonable period. It is also important because, if a patient's skin is thoroughly healed, he is more apt to remain well when he returns to work. If a man's former work involved contact with sensitizers which led to a dermatitis, then he should be advised not to return to that work. If he has been injured by a recognized primary irritant he should avoid that substance or handle it with proper respect, so that he can frequently return to his former occupation with impunity.

There would be fewer disputed cases before the industrial accident board if the courts accepted the fact that the compensation act provides for disability only. What holds for a strained back should also hold for an occupational dermatitis, as was demonstrated in Borstel's case, 307 Mass. 24, where the Supreme Court ruled that, despite the fact that the man had previous injury to his back, the final act which produced disability was his work at his last place of occupation, and therefore found that the last insurer should assume liability. However, the chief objection to this is that it would be absolutely necessary entirely to relieve a patient from his occupational dermatitis before he resumed any type of work, and would result in employers refusing to accept or hire an individual suffering from any type of rash. This would, of course, prevent numerous workers from resuming work, for there is no question that a slight eruption does not always disable an individual from doing work that does not involve contact with irritants. Therefore the board continues to rule on the particular facts in each case individually, and the State Supreme Court treats each case on its own merits. There is no uniformity —perhaps not even any consistency—in the decided cases.

Aggravation

Aggravation of preexisting disease through an occupational injury should be compensated only for the period of time during which the aggravation is actually and entirely caused by the injury. One should try to determine the disability due to the compensable injury and that which is due to the preexisting disease. If the patient stops work, and if the effect of the injury on the preexisting dermatosis has been eliminated, and if treatment has resulted in relief of the superimposed occupational dermatitis, compensation is no longer justified. The problem becomes still more involved if the preexisting disease, such as psoriasis, is a progressive one. The difficulty then is to decide when the preexisting disease has reached the stage which it would have reached without the influence of an injury. During this period the disability is also pro-

gressive. There may be no justification for further compensation because the role of the occupational dermatitis as a contributing factor has ceased—however, most of these cases are awarded compensation for the entire disability, primarily because of conflicting testimony as to when, if at all, the aggravation has ceased.

Apparently no hard-and-fast rule or formula can be applied to the word aggravation. The exact conditions of each individual case produce a decision peculiar to that case. From a large number of such cases, however, certain concepts with wide border lines may be derived. If a workman has had psoriasis for many years prior to engaging in an occupation, during the course of which his psoriasis has become worse, so severe that it involves his hands with a result that he has been unable to continue at that particular occupation, which may or may not be an aggravating factor, he usually sues for compensation. He claims that the disability which eventuated was an industrial injury.

In such a case in Massachusetts psoriasis of the palms developed in an edge setter after he had been working for 10 years. In the performance of his work, the edge setter painted the edges of the soles of shoes with a blacking compound and then pressed the edges against an electrically heated, vibrating iron. About six months after the onset of the eruption on the palms, psoriatic areas also developed on the plantar surfaces. The edge setter was examined for the insurer, and an opinion was expressed that the condition was psoriasis not of occupational origin. The decision of the Massachusetts Industrial Accident Board on his claim for compensation was that "the employee . . . sustained an injury that arose out of and in the course of his employment" and that "as a result of this injury he was totally disabled for work" for 13 weeks. Fourteen years later, this same worker was again referred for examination and opinion, this time by a different insurer for a different employer. Although there had been some variations in the intensity of the eruption, it had never been completely clear during this interval of time. The edge setter worked for the first employer for about two years after the first industrial claim. Thereafter, he worked for six different employers, doing essentially the same type of work. The Board describes the interval of approximately 13 years in these words: "The employee has persistently pursued the same type of employment in the shoe industry, namely, edge trimming and edge setting, and notwithstanding that he has suffered intermittent repeated exacerbations and remissions of cracked and swollen hands, principally on their palmar surfaces, with rash, scaling, and redness, when the condition was acute and severe. . . ."

A dermatologist called as a witness by the employee at the last hearing testified that "the work as an edge trimmer and edge setter aggravated the basic condition of psoriasis." One impartial dermatologist expressed the opinion to the Board that the employee "has an eruption which is psoriasis," and that this is "a constitutional disease in which trauma 'can be' the 'initiating' cause"; he also believed that "continued work handling stains, shoes, and other ingredients 'could' aggravate his (the edge setter's) psoriasis." Another impartial dermatologist consulted by the Board expressed the opinion that "the condition which the employee suffers is psoriasis and is in no way causally related to his employment at any time." The full Board, in their findings after review, made the following statement:

> We prefer to follow the opinion . . . that the condition which the employee has suffered is one of psoriasis, a non-industrial disease, that such disease has not been aggravated by any of the employments against which claim is made on the record. . . . We find that the employee has not sustained the burden of proving that he has received a personal injury arising out of and in the course of his employment in the service of any of the employers against whom claim is made subsequent to the 1936 episode. We find further that the employee's incapacity beginning on September 9, 1949 is not causally related to his 1936 injury.

Here apparently are diametrically contradictory opinions by the same Board for the same employee, suffering from the same and continuing condition of psoriasis while engaged in the same industry. The two hearings differ from each other in that different employers are involved; they also differ in a matter of jurisdiction regarding one of the employers because of location in another state.

Appel [12] states that an analysis of a large number of industrial dermatitis cases in which the factor of aggravation played an important part permitted all the cases to fall into one of the following five categories: industrial dermatitis (1) aggravated by a supervening nonindustrial condition; (2) aggravated by a supervening other industrial condition arising out of and in the course of employment for the same employer; (3) aggravated by a supervening other industrial condition arising out of and in the course of employment for a different employer; (4) aggravated by a preexisting nonindustrial condition; (5) itself aggravating a preexisting nonindustrial condition.

If a patient is accepted as being disabled as a result of aggravation of his nonindustrial dermatitis, then the physician must try to discriminate between the natural development of the nonoccupational eruption and the disturbances caused by the injury received at work and should be able to determine when the results of the aggravation have ceased and only the preexisting disease remains. If the patient had suffered from a clearly defined systemic cutaneous disease, such as psoriasis or syphilis, this decision is fairly easy. For example, if a man suffers an injury to his leg and then develops a localized patch of psoriasis, he should receive treatment only until this patch is relieved. The same is true regarding a gumma resulting from

injury. However, such an injury as in the case of the loss of the sight of both eyes in a patient with syphilis might result in total permanent disability.

The latter was shown in the case of Nicotra vs. Bigelow, Sanford Carpet Co. (Conn., 189 A.603).[13] The claimant, while at work cleaning the inside of a metal tank with an electric brush, complained to a fellow worker that something had got into his left eye. Shortly afterward the claimant reported to the plant surgeon, who found some pieces of foreign matter in the eye, which he apparently removed. The claimant, however, continued to insist that there was still something in his eye, and during the next several months he received treatment from various physicians but obtained no relief. Eventually he became totally blind in his left eye. Vision in his right was reduced to less than one-tenth of normal vision and the condition could not be corrected by lenses. During the course of treatment for his eye condition it was discovered that the claimant had syphilis and he underewent treatment for that disease. In a proceeding under the workman's compensation act of Connecticut, the commissioner awarded the claimant compensation and the employer appealed to the superior court, which remanded the case to the commissioner for the taking of further evidence. The claimant thereupon appealed to the Supreme Court of Errors of Connecticut.

The commissioner concluded that an injury which the claimant received to his left eye precipitated an optic neuritis in that eye and that atrophy of the optic nerve developed, resulting in total blindness in that eye; that sympathetically the right eye was affected by the injury to the left, so that the net results of the injury was that the claimant was industrially blind in both eyes. The employer contended that it was error for the commissioner to receive the statement in evidence. The contention, the court said, overlooks the nature of the hearing before the commissioner. The law provides that the commissioner shall not be bound by the ordinary common law or statutory rules of evidence or procedure and is therefore permitted great latitude in the admission of evidence. The employer further contended that an award of compensation to the claimant was not permissible because the workmen's compensation act provides that in case of an accidental injury a disability or death due to the acceleration or aggravation of syphilis does not constitute a compensable injury. Under this provision, the court said, where the effect of the injury is to accelerate or aggravate the constitutional disease, no recovery can be had. In the present case the ultimate conclusion of the commissioner was that the injury which the claimant received because of his condition affected the optic nerve in such a manner as to result in loss of sight of both eyes. As the record supported this conclusion, the court said, the disability was compensable. The case was remanded to the superior court, with directions to enter judgment for the claimant.

Disfigurement

Another problem coming before the industrial accident boards is disfigurement. Previously it was considered not compensable. A case [14] was reported in which the claimant's face was badly scarred by acid, resulting in considerable disfigurement. He was not otherwise injured and instituted proceedings under the workmen's compensation act of New Jersey. The question as to whether or not disfigurement constituted a compensable disability eventually was presented to the Supreme Court of New Jersey. A reading of the several sections of the workmen's compensation act, said the court, clearly indicates a legislative purpose to provide compensation for disability which disqualifies an employee from doing work in whole or in part. In De Zeng Standard Co. v. Pressey, 86 N. J. Law 469, 92 A. 278 (affirmed in 96A.1102) the court said: "The disability intended thereby (the act) is a disability due to loss of a member, or part of a member, or of a function, rather than to mere loss of earning power." In that case it was claimed that if there was injury but no loss of actual wages there was no loss of earning power, and that this precluded an award. The court, however, refused to take this view, declaring that it was disability alone that counted, whether loss of physical parts or loss of function. In the present case the court said that the disfigurement and scars on the claimant's face may well deter employment and thereby lessen his earning power, but they in no wise impair his ability to work. If disfigurement, standing alone, is to be made the basis of compensation, it must be done by the legislature and not by an extension of the act by judicial construction. If and when such legislation shall be deemed desirable, the court said, the legislature can determine what types of disfigurement, marks, and scars, and on what portion of the face, head, or body, shall be considered, and within what limits and bounds awards of compensation shall be made.

However, Bear [15] later cites a case tried before the Massachusetts Industrial Accident Board, L. Hendricks v. Chesterfield Laundry Service Company. This employee was a 31-year-old woman who was operating a laundry pressing machine. A part of the machine weighing about 50 lb. shut down on her right forearm, burning her. She managed to free herself and then fainted. After treatment, a granulating surface was obtained. The large open surface was filled in with skin grafts. This graft took fairly well, except that where it crossed the wrist joint there was some stiffness and cracking due to the motion of the joint at that point. The important feature of the case, however, was that the patient was left with an extensive keloid formation, which disfigured her arm. The employee testified at the

hearing that she was sent from an employment agency to two different families to do housework. The prospective employers kept looking at her arm, and the agency was notified after each interview that she had not been hired because the scar was considered obnoxious. The commissioner found that this constituted a disability and awarded compensation, which the insurer paid without appeal to the courts.

Patch Tests

Testimony concerning the value of patch tests at hearings before industrial accident commissions may be a great tribulation to a conscientious physician. He must perform and interpret the test himself; otherwise, it is hearsay evidence and therefore irrelevant. It is difficult for the physician to explain a negative reaction, when he is certain that the patch test did not simulate the conditions under which the employee's skin was exposed to the irritant. On the other hand he cannot explain an apparently positive reaction appearing at the site of the test, when it could be merely another patch of a spreading eruption that involved the test site. Lawyers and commissioners have difficulty understanding false-positive, false-negative, and delayed reactions to patch tests.

Among the legal questions which occasionally confront the dermatologist who investigates cases of industrial disease are those which arise when a patch test is performed that causes a severe and possibly disabling dermatitis. An opinion was requested from the Massachusetts Industrial Accident Board [16] regarding the liability of the physician to the claimant, the liability of the insurer to the claimant, and the rights of the claimant over the physician and the insurer. The Board's reply was intended to furnish helpful information and not to set forth the law.

On June 14, 1940, Mrs. F. at her employer's request removed a ladder from under considerable brush. In so doing she was showered with a pollen-like substance, which covered her head, face, neck, and arms. That night her face grew red and itchy and later burned. The next day it was erupted and swollen. She received medical treatment and was confined to the house for seven weeks. Even after that time itching and burning continued, and red patches appeared on her face whenever it was exposed to heat. When first examined on Aug. 20th, her skin was normal except for slight erythema of the face. She was accompanied by an inspector of the Massachusetts Department of Industrial Accidents; he brought with him specimens of four plants like those with which the patient came in contact and requested patch tests. These tests were performed on the flexor aspect of the left forearm with a minute piece of each plant. Within a few minutes the patient complained of itching, and an area of redness was observed surrounding the test piece of a plant called by the patient a Chinese plant. Despite removal of the substance and cleansing with soap and water and alcohol, the redness continued to spread and covered an area 4 in. (10 cm.) square. The other patch tests were negative. On Aug. 21st the patient returned with a dermatitis of the left forearm.

The results in the above case aroused interest anew in certain legal questions to which such results give rise. Is one justified in performing a patch test that may cause an aggravation or, if the patient is well, a new and disabling dermatitis? Is the one who requests the test or the one who performs it liable for such disability? Should the consent of the insurer to the test be secured as well as that of the patient? Was one justified in undertaking treatment of the patient during the illness that ensued? Who should pay for this treatment, the state or the insurer? If the patient had been disabled by the dermatitis caused by the patch test, would she have been entitled to further compensation?

To a letter presenting these questions, the Board replied that since in performing the patch test the physician was acting under appointment by an administering board with legislative permission so to appoint and since it was a procedure generally endorsed by the medical profession, he should probably be immune from suit by the insurer and certainly immune from suit by the employee (as held by the Mass. Supreme Court in the case of Vatalero vs. Thomas, 262 Mass. 383). The Board pointed out that in view of its having appointed him, his position was neither that of physician to the employee nor physician to the insurer. As to the employee's right to further compensation for an aggravation and extension of the original dermatitis, the Board cited the fundamental principle that the insurer is liable for all the consequences which flow "as a rational result" from the original injury. Among these consequences it included any conditions resulting from examination and treatment by any physician, whether impartial or employed by the employee or insurer, provided that these were properly conducted and were recognized procedures. In connection with the Board's reply, a private legal opinion was solicited while the patient was still under treatment. This opinion was that there is no liability on the part of a dermatologist unless he is negligent in treatment and that he is therefore under no obligation to obtain permission from any one to perform a patch test. In the case of a subsequent eruption, it was held, the insurer would be liable for disability, if any, since examination by an impartial physician is provided for under the Workmen's Compensation Act.

Cost

A dermatitis case can be quite expensive. The following case, while somewhat unusual, illustrates this point and also directs attention to one of the principal

causes of prolonged dermatitis—overtreatment. On Oct. 18, 1949, a man 50 years of age was referred by an insurance carrier for examination of a dermatitis resulting from contact with cutting oils used in his work as a metal worker. The eruption started the previous April on the anterior aspect of the thighs, later involving the wrists and forearms. In December, 1949, he was referred back for therapy, for his eruption had become generalized in spite of x-ray therapy, injections of penicillin, and various other medication. He was hospitalized with marked improvement, although the pruritus persisted. Contrary to advice he continued using various home remedies. In October, 1951, at the request of the insurer he was seen at a suburban hospital where his own doctor was treating him. A month later a local physician referred him to a large teaching hospital. Here he was placed under the care of an internist who was specializing in steroid therapy, which was then both experimental and very expensive. Cortisone therapy was started on Dec. 2, 1950, and he remained on steroid therapy under the care of this internist until a short time before his death on Nov. 16, 1954. At first he made excellent progress as regards his skin, but he soon showed untoward reactions each time the drug dosage was lowered or withdrawn. He had a total of 14 hospital admissions. The total medical cost in this case [17] was reported to be $34,014.25. The compensation paid over a period of five years was $8,758.57. His widow 54 years of age is now being paid $15 a week for life, so that another $15,600 expenditure is expected, making a total of $58,000.

Rehabilitation

For an employee, disability creates a problem which will vary in degree according to the occupational or nonoccupational character of the ailment, the age of the worker, the length of time in the particular trade, and the accumulated seniority within the company. If he or she is a beginner in the employment and if the trouble is ruled as work-associated, the illness is covered by compensation. In such a case transfer to another department or separation from the job will not cause loss of the higher wage scales gained after long experience.[18] However, when a man has learned a highly specialized trade, such as engraving, and he becomes disabled because of skin irritants, he is of no value to his employer or to others in any job involving contact with skin irritants. Although he is compensated for this episode, he still faces the penalty of a lowered income. This results from the necessity of a plant transfer to another job in which he has no trained skill, or severance from the position in which he has developed efficiency and seniority. Lost time which is not covered by any type of benefits can be catastrophic to him and his dependents.

The trained artisan will frequently, and with some justice, decide that his disability, no matter how slight, has a certain monetary value. Workers may demand a high price for a dermatitis of one finger which does not disable them from ordinary work, but may eliminate them from their trade. They are apt to prolong this dermatitis until they are given a lump sum settlement, with the result that the patient is not so much interested in his physician's effort to restore him to work as he is in his financial settlement. On the other hand, occasional attempts may be made to deny a worker's just claim or to settle a claim more cheaply in a lump sum which terminates an employer's liability for compensation.

Lack of rehabilitation services and inadequate medical care may result in prolonged disability and unnecessary loss of gainful employment, as well as an occasional neurotic, permanent invalid. After the acute disabling symptoms of occupational dermatitis are relieved, work away from contact with irritants should be found. Rehabilitation through vocational training may be necessary.

This aspect of disability is relatively new as compared to the problems of prevention and compensation of occupational dermatoses. There is no uncertainty about its importance, because rehabilitation provides a means of reestablishing the vocational and economic usefulness of the skilled worker who, by virtue of his cutaneous susceptibility, must change type of work. Real recognition for the need of rehabilitating the disabled workman is evident, for at this time about 23 states have certain provisions dealing with rehabilitation. When physicians are confronted with the need for rehabilitation of a patient with a dermatosis, they should confer with the employer and the insurance company or consult their state departments of health, or workmen's compensation office, or departments of labor to ascertain whether a rehabilitation activity is available within the state.

Conclusions

It is the duty of all physicians to care for the sick. Workers suffering from occupational dermatoses are sick and need proper care. Some specialists have been reluctant to take compensation cases. They claim they are ignorant of the law, lack medicolegal training, fear legal interrogation, and believe the fees are so low that expenditure of their time is not properly compensated. If a physician undertakes the care of the patient, it is his duty to appear and testify. Knowledge of the workings of the compensation act is desirable. The physician should realize that he is not beholden to anyone. The position of the dermatologist is that of a physician trained in the diagnosis and treatment of cutaneous disturbances. He has sufficient knowledge to recognize whether or not it is systemic in origin, or due to extrinsic factors. If due to the latter, and a careful history reveals the probability of occupational factors,

an honest statement of the facts can withstand any direct or cross-examination to destroy his opinion. If a careful history narrows the field of probable causative factors necessitating the aid of the patch test, the dermatologist should not hesitate to employ such diagnostic aids.

His testimony should be independent of his lawyer, the plaintiff, or the defendant; in court he is not an agent of either, but subject only to the ethics of his profession. He should not be partial or prejudiced to either side. Antagonism by a lawyer for either side is quickly recognized (and usually remedied by the presiding officer) and often is a deciding factor in the decision. The physician should be able to recognize the extent of disability and the prospect of the worker's recovery. Proper cooperation between the dermatologist, the employee, the employer, and the compensation administrator will help to reduce the number of controversial cases. The intent of the compensation act is just and humane and is entitled to the cooperation of all concerned.

The Committee wishes to express thanks to Mr. Joseph Bear for his review of the legal questions involved in this paper. The Committee also wishes to acknowledge the contribution of Dr. John G. Downing, former Chairman, in the preparation of this paper.

References

1. State Workmen's Compensation Laws. Bull. 161, U. S. Dept. of Labor, Washington, D. C., August, 1957.

2. Bulletin 13, State of Connecticut, 1935.

3. Sappington, C. O.: Medicolegal Trends in Occupational Diseases; Statistical and Legal Analysis of Medicolegal Experience, Indust. Med. **6**:229-242 (May) 1937.

4. Downing, J. G.: Legal Aspects of Industrial Dermatoses, New England J. Med. **215**:577-580 (Sept. 24) 1936.

5. Supreme Judicial Court. McCann, 1934, 286, Massachusetts, 541.

6. Workmen's Compensation Acts: Permanence of Cinnamon Sensitivity, Bureau of Legal Medicine and Legislation, J. A. M. A. **140**:1596 (August 23) 1952.

7. Mere Allergic Condition Not Compensable, Bureau of Legal Medicine and Legislation, J. A. M. A. **122**:58-59 (May 1) 1943.

8. Compensability of Disability from Idiosyncrasy to Soap Required to Be Used in Course of Employment, Bureau of Legal Medicine and Legislation, J. A. M. A. **123**:991-992 (Dec. 11) 1943.

9. Downing, J. G.: Dermatologist and Industrial Accident Board, Indust. Med. **14**:653 (Aug.) 1945.

10. Supreme Judicial Court. Maloff, 276, Massachusetts, 610. Supreme Judicial Court. Pantagotopulus, 276, Massachusetts, 600.

11. Supreme Judicial Court. Wentworth, 284, Massachusetts, 479.

12. Appel, B.: Aggravation as Factor in Industrial Dermatitis, A. M. A. Arch. Indust. Hyg. **8**:133-142 (Aug.) 1953.

13. Workmen's Compensation Acts: Blindness in Relation to Trauma and Syphilis: Medical Books in Evidence, Bureau of Legal Medicine and Legislation, J. A. M. A. **109**:901-902 (Sept. 11) 1937.

14. Workmen's Compensation Acts: Disfigurement Not Compensable Disability, Bureau of Legal Medicine — Legislation, J. A. M. A. **109**:902 (Sept. 11) 1937.

15. Bear, J.: Personal communication to the committee. Cited in Compensation Act and Dermatologist, Compens. Med. **2**: (Nov.) 1949.

16. Bear, J.: Legal Aspects of Patch Tests, Arch. Dermat. & Syph. **44**:63-65 (July) 1941.

17. Morris, G. E.: Failure of Steroid Therapy in Contact Dermatitis, Indust. Med. **24**:538-540 (Dec.) 1955.

18. Dalton, J. E.: Industrial Dermatoses, Indust. Med. **22**:167-171 (April) 1953.

COMMITTEE ON MEDICOLEGAL PROBLEMS

INTERPRETATION OF TESTS FOR INTOXICATION

Ralph F. Turner, M.S., East Lansing, Mich., Herman A. Heise, M.D., Milwaukee
and
Clarence W. Muehlberger, Ph.D., Lansing, Mich.

This report is chapter 6 from a manual, being prepared by the Committee on Medicolegal Problems, dealing with medical and legal procedures involved in the use of chemical tests for intoxication.

Popular beliefs regarding the effects of alcohol do not agree with the scientifically conducted observations. We have all heard of the mythical individual who "smells the cork" and becomes dead drunk, while another is cold sober after downing a "fifth." Actually the startling fact is that alcohol affects human beings in a surprisingly uniform manner when we measure, not how much the person drinks, but how much he accumulates in his body fluids. This uniformity is demonstrated by observing that the threshold for measurable effects of alcohol usually occurs at a blood alcohol level of about 0.02 to 0.03%, indicating the accumulation of 0.4 oz. (12 cc.) to 0.6 oz. (18 cc.) of pure alcohol in a 150-lb. (68-kg.) person. The fatal dose also is no respecter of persons. When a person accumulates enough alcohol to have a blood level of 0.6%, his most primitive nerve functions are interfered with and he dies.

Evaluation of Tolerance

It is true that habituation to alcohol alters these figures slightly, but the importance of tolerance has been greatly overrated. While the tolerant person may be able to drink more than the novice, the two will be about equally intoxicated when they accumulate the same amount of alcohol. The tolerant individual may eliminate his alcohol faster and absorb it slower. It is also possible that what we regard as tolerance may actually be an ability, acquired by practice, of hiding some of the symptoms of intoxication. For example, the often intoxicated individual may have learned to talk softly, to enunciate clearly, and to drive with exasperating slowness. It should therefore be understood that the chemical test for alcohol is just, since it measures not how much the person drank but what he accumulated, and it is the accumulated alcohol that causes intoxication.

If the above statements are true, why then are we confronted with apparent contradictions? How can we explain that, of two persons of about the same age, height, and weight, both charged with driving while intoxicated, both having 0.15% alcohol in their blood, one is polite, cooperative, and well oriented while the other is profane and combative? The explanation for this apparent paradox has been found by the testing of hundreds of individuals before and after taking alcohol. It can then be shown that there is a great natural difference in persons. The intelligent person accustomed to the successful handling of himself in difficult situations will appear to be less affected by alcohol than the scatterbrained person whose blood contains the same percentage. The experiments indicate that the two persons, though reacting differently, are about equally removed from their own normal behavior patterns.

It has therefore been suggested that the superior person be judged by a more lenient standard than that imposed on his less fortunate brother. We feel, however, that this attitude is not reasonable or feasible, since driving even without alcohol is such a hazardous occupation that any reduction in driving ability caused by alcohol should not be countenanced.

Effect of Suprarenals

Another interesting observation is that a person may have been obviously intoxicated, but when he is confronted by the police or being examined by a doctor suddenly appears to be sober. What has happened is that the realization of his predicament has caused his suprarenal glands to secrete large quantities of epinephrine, which temporarily counteract the effects of alcohol but not the percentage in his body fluids. When this person believes that the emergency has passed, he again relapses to his observable state of intoxication. This temporary, apparent sobriety can be compared to what happens to the sleepy individual whose house catches fire. As soon as he realizes what is happening he is wide awake.

When we consider the variety of symptoms, or even the temporary absence of symptoms associated with alcoholic intoxication, it is fortunate that we have available one constant finding which enables us to evaluate properly the role of alcohol as a factor in abnormal behavior. This was dramatically demonstrated by Halporn [1] when he was able to prophesy with surprising accuracy the percentage of alcohol which would be found in the urine of persons whom he had examined. His very worst estimate was 0.30% in a person whose actual percentage was only 0.18. Later on it was discovered that this person had a fractured skull, indicating that the chemical test was an even better diagnostic tool than the physical examination alone.

What Is Intoxication?

In order to interpret the results of chemical tests for alcoholic intoxication, it is obvious that we must define intoxication. This condition has been considered to be present according to some authors only when there has been obvious mental confusion and/or muscular incoordination, while others have considered that a person is under the influence of alcohol as soon as only slight measurable neurological deterioration can be demonstrated. The same person simultaneously examined by two doctors may be considered culpable by one and innocent by the other, depending on the doctor's criteria for intoxication.

It is obvious, then, that all arguments are fruitless unless we agree as to what is meant by "under the influence." We are in favor of any definition which adequately describes this condition and which can be used to convict the guilty and free the innocent. The same definition should apply in all states and preferably in all countries. At the present time we have many definitions of intoxication. To be guilty in California the individual must be so affected that he is unable to operate his vehicle in the manner of an "ordinarily prudent and cautious person in full possession of his faculties." Dr. Henry Newman correctly interpreted this to mean that a person should not be penalized unless the alcohol had lowered his driving ability below that of the poorest licensed driver on the road. According to this definition it is extremely difficult to prove intoxication. The California law exonerates the superior individual who in spite of some loss of his driving ability due to alcohol is still a better driver than most ordinary drivers.

On the other hand this superior Californian would not fare as well if scrutinized according to the laws of Arizona. Because of the difficulties of proving "under the influence" of alcohol, the Na-

tional Safety Council and the American Medical Association have urged the adoption of the following definition of the Supreme Court of Arizona:

> The expression "under the influence of intoxicating liquor" covers not only all the well known and easily recognized conditions and degrees of intoxication but any abnormal mental and physical condition which is the result of indulging in any degree in intoxicating liquors, and which tends to deprive him of that clearness of intellect and control of himself which he would otherwise possess. If the ability of the driver of an automobile has been lessened in the slightest degree by the use of intoxicating liquors, then the driver is deemed to be under the influence of intoxicating liquor. The mere fact that the driver has taken a drink does not place him under the ban of the statute unless such drink has some influence upon him lessening in some degree his ability to handle said automobile. *Steffani v. State*, 42 Pac. (2nd) 615.

A. M. A. Recommendations

The following recommendations were agreed on by committees of the National Safety Council and the American Medical Association:

1. Although there is no minimal figure which can be set at which there will be absolutely no effect from alcohol, the committee recommends that persons with a concentration of alcohol of less than 0.05% by weight in blood or its equivalent in urine, saliva, or breath should not be prosecuted for driving while under the influence of alcoholic liquor.

2. Between 0.05 and 0.15%, a liberal, wide zone, alcoholic influence usually is present, but courts of law are advised to consider the behavior of the individual and circumstances leading to the arrest in making their decision.

3. At 0.15%, or above, there is definite evidence of "under the influence," since every individual with this concentration would have lost to a measurable extent some of that clearness of intellect and control of himself that he would normally possess.

These limits were purposely made liberal so that no injustice would be done to the person with unusual tolerance. In order to obtain a blood alcohol level of 0.05%, a 150-lb. (68-kg.) person would have to accumulate 1 fl. oz. (30 cc.) of pure alcohol in his body. To do this he would have to drink at least the equivalent of 2 oz. of 100-proof liquor. This same person would have to accumulate 3 oz. of absolute alcohol to reach a blood alcohol level of 0.15%.

The proper interpretation of chemical test results is based on an assessment of the relative importance of conflicting social values rather than the determination of scientifically established facts.

There is little doubt that some deterioration of human capabilities is observed at very low levels of alcohol concentration in the circulating blood. If this were evident a quarter of a century ago,[2] the more sensitive and carefully controlled experimentation of modern times [3] has only served to provide additional evidence that some measurable loss of human capacities occurs after only one of two drinks (blood alcohol levels of 0.02% to 0.03%). Thus, if we were interested only in maximum safety on the highway, we would adopt the rule, "If you drive, don't drink."

One of the cornerstones of our American way of life is the element of personal freedom, the maximum liberty of the individual to do as he pleases within the restrictions of majority-approved laws. When personal freedom is too rigorously trampled on by a restraining statute, our citizenry are likely to nullify the law by refusing to abide by its provisions. For this reason the value of any regulation depends on general public acceptance of its fairness. The fate of the 18th amendment to our constitution serves as a good example of this point. Thus, any reasonable regulation concerning drinking and driving involves a steering between the Scylla of blue-nose restriction and the Charybdis of extreme libertarianism.

It would seem that a fair degree of latitude of individual freedom is permitted if we bar only those drivers in whom the alcohol-induced impairment is material. By that is meant: noticeable to any alert observant citizen and manifested by obvious interference with locomotion or balance (standing, walking, or turning), speech (indicated by slurred pronunciation or blocking of speech), or orientation (as indicated by mental confusion as to time, place, or circumstances).

Leniency of Recommendations

Realizing the wide range of human variability and tolerance with respect to the effects of alcohol, it seemed only fair to establish two limits, a minimum or floor value and a maximum or ceiling value for the blood alcohol concentration indicating material impairment—the floor value to be that concentration below which the vast majority of persons demonstrate no material abnormality and the ceiling value to be that concentration above which all persons are materially impaired.

Such delineation of zones of no influence and definite influence in all persons would necessarily leave a rather considerable middle zone in which some persons might be materially impaired whereas others could be reasonably normal. This represents a doubtful zone between the two definite floor and ceiling values.

In setting out to establish reasonable and fair limits for alcohol influence, the question first asked was: "Below what blood alcohol concentration can we safely say that no person would be materially impaired in those factors which are essential for the safe operation of a motor vehicle?" Although delicate tests are able to demonstrate impairment at blood alcohol concentrations of 0.02% to 0.03%, it was agreed that material impairment by alcohol

was not observed in any person until the blood alcohol level rose to 0.05%. So this was selected as a reasonable floor value.

The adoption of a defensible and fair ceiling value was made only after much discussion and some controversy. Because a noticeable impairment could be seen in the great majority of persons at a blood alcohol level of 0.11%, it was first suggested as a ceiling value.[4] However, there are a few tolerant persons (mostly habitual users of alcoholic beverages) in whom no noticeable degree of impairment can be seen at a blood alcohol level of 0.11%. But even these show observable impairment by the time a blood alcohol concentration of 0.13% has been reached. Realizing that not all persons had been tested and that somewhere some person might be found who was still more tolerant than any seen by American experimenters, and further recognizing the fact that even skilled analysts might differ in the measurement of blood alcohol values by a margin of ± 0.01%, it was decided to place the ceiling value at 0.15% in order to make allowance for these unknown factors.

Thus the 0.15% ceiling value is recognized as one which is inordinately high and extremely conservative—a deviation which was considered to be fair in the light of our tradition of justice, wherein it is believed to be better for a guilty man to go free rather than have an innocent one convicted.

These values recommended by the committees of the National Safety Council and the American Medical Association have been found to be preeminently fair and even generous.[5] In the countries of Western Europe the limiting values are more stringent. Norway and Sweden have adopted 0.05% as the blood alcohol limit which may not be exceeded by motorists. In Denmark, Germany, and France, the limit is one part per thousand or 0.10%. So the ceiling value of 0.15%, recommended in the Uniform Vehicle Code and adopted into the statutes of 28 of our states, is in keeping with our American tradition of permitting the maximum freedom for the individual which does not interfere materially with public safety.

Suggestions have been made that, in view of saving some of the 40,000 lives which are lost annually in highway accidents, the ceiling value be lowered to 0.05%.[6] This would be tantamount to forbidding any person who has in his body alcohol equivalent to two bottles of beer from driving an automobile. It is doubtful if such a rigid limit could be enforced.

A False Interpretation

All too frequently one finds that, where chemical tests for intoxication are employed, prosecutors or judges take the position that no person with less than 0.15% alcohol in his blood should be prosecuted, regardless of the symptoms of intoxication which he may manifest. This is a perversion of the intent of the chemical testing program. Certainly where indications of alcohol influence are evident and where no element of injury, illness, or medication suggests other causes for the driver's condition, the finding of a blood alcohol concentration in the questionable zone (between 0.10% and 0.14%) justifies the bringing of a prosecution for "driving while under the influence of intoxicating liquor."

Conclusions

It is, of course, understood that the blood alcohol concentration indicates the condition of the person at the time the test was taken. What his blood alcohol concentration was at the time of the arrest or accident can be inferred with reasonable accuracy if one can establish by interrogation the time of drinking (including the time drinking commenced, the time of the last drink, and the subject's best recollection of how much liquor was consumed). It has been argued that such extrapolations are conjectural and should not be admitted in evidence. But where the chemical test has been made within one or two hours after the arrest or accident, and facts concerning the drinking are established, courts have held such extrapolations to constitute the best available evidence and, or that basis, to be admissible.[7]

When chemical tests for intoxication are properly made and interpreted in accordance with the principles outlined above, they constitute the best and most impartial objective yardstick for the measurement of impairment by alcohol. Recognition of this fact led our highest court to state (of a blood alcohol test in a negligent homicide case) "The test upheld here is not attached on the ground of any basic deficiency or of injudicious application, but admittedly is a scientifically accurate method of detecting alcoholic content in the blood, thus furnishing an exact measure upon which to base a decision as to intoxication."[8]

References

1. Heise, H. A., and Halpron, B.: Medicolegal Aspects of Drunkenness, Pennsylvania M. J. **36**:190-195 (Dec.) 1932.

2. Miles, W.: Psychological Effects of Alcohol in Man, in Emerson, H., and others: Alcohol and Man: Effects of Alcohol on Man in Health and Disease, New York, the Macmillan Company, 1932, p. 259.

3. Loomis, T. A., and West, T. C.: Experimental Study for Evaluation of Some Medicolegal Aspects of Influence of Alcohol on Automobile Driving, Quart. J. Stud. Alcohol, to be published.

4. National Safety Council: Chemical Tests for Intoxication, Report of Committee on Tests for Intoxication to Street and Highway Traffic Section, Chicago, Ill., 1938.

5. Heise, H. A.: Committee to Study Problems of Motor Vehicle Accidents, Report of Officers, Organization Section, J. A. M. A. **124**:1290-1292 (April 29) 1944.

6. Motor-Vehicle Accidents, Organization Section, J. A. M. A. **163**:1149-1150 (March 30) 1957.

7. Donigan, R. L.: Chemical Tests and Law, Evanston, Ill., Traffic Institute, Northwestern University, 1957.

8. *Breithaupt v. Abram*, 352 U. S. 432 (1957).

MEDICINE AT WORK

- *Big PG Course—Via AMA*
- *Rehabilitation Moves Ahead*
- *Medical Education Reports*
- *Session with 'Third Party'*
- *Extent of Group Practice*
- *Medicine's 'Up' Frontier*
- *SPECIAL REPORT IN DEPTH —The Troubled Employee*

More People Prepay

"Public acceptance of the idea of preplanning and budgeting some of the costs of illness, injury and disability has been proved by the continued increase in enrollment under voluntary health insurance plans." That is the conclusion of a pamphlet issued recently by the A. M. A. Council on Medical Service as a supplement to its booklet, "Voluntary Prepayment Medical Benefit Plans."

Although the number of voluntary health insurance plans in the U. S., approved by medical societies, reached a peak of 84 in 1951, enrollment in these plans has continued to climb at an average rate of nearly 4 million yearly. Total enrollment neared 45 million by the end of 1957. On Dec. 31, 1945, it was less than 3 million.

The pamphlet says: "Growth in numbers of persons alone does not indicate the full story. The basis of payment of many programs has been expanded . . . and the amounts of many benefits have been adjusted so as to be more in keeping with economic trends."

The number of plans approved by medical societies has varied from state to state. Washington has 24; New York and West Virginia, 8 each; Texas, 2. Most have only 1.

Physicians cluster around "live" demonstration at one of the Scientific Assembly's special exhibits on fractures, an annual favorite.

A. M. A. Scientific Assemblies

Great 'Show and Tell' Sessions Offer Advanced Education in a Physicians' Forum

The art of anesthesia had hardly emerged from the "laughing gas" era when the American Medical Association held its first annual meeting in Baltimore in 1848. But concerned though they were with organizational problems, the assembled physicians took time to listen to Dr. J. C. Warren of Boston, generally credited with being the first man to operate on a patient under ether anesthesia.

Dr. Warren not only told the small group of his experience but set a pattern for future meetings when he illustrated the method of preparing chloric ether. The pattern, with modifications, still holds today—108 years later.

Physicians attending the Clinical Meeting in Minneapolis next month will be seeking information and will get it from confreres who will be using modern adaptations of Dr. Warren's "show and tell" method.

The Clinical Meeting, established 10 years ago as an outgrowth of the Annual Meeting, is similar to it in content and presentation. Designed to appeal especially to the general practitioner, it will again offer a condensed postgraduate course in medicine by means of essays, exhibits, motion pictures, and color television.

Despite Dr. Warren's pioneering, the standard medical "paper" was the chief means of communicating information at Annual Meetings during the first half century of the A.M.A.'s history, but an 1899 innovation brought a marked change in emphasis. In that year, two Indiana physicians arrived at the Columbus, Ohio, session bearing jars of pathological specimens.

Renting, at their own expense, a warehouse near the meeting place, the two put their labeled specimens on display and lured their fellow doctors to the exhibit.

Their efforts were so well received that, by resolution, the A.M.A. decided to make similar displays an annual affair. The impact of the pathology exhibit was so great that, in 1902, the format was expanded to include all areas of medicine.

The two Hoosiers with their box full of wet specimens would be amazed at how their child has grown. At the Annual Meeting in San Francisco last year, 325 colorful, lighted displays of medical information were ranged aisle-on-aisle on the floor of the convention hall. Each had

been carefully thought-out, planned, constructed, and shipped by a single physician or group. Each had survived a competitive screening that eliminated 200 more. The sole reward of the exhibitor was to be allowed to spend his convention days manning his display and answering hundreds of questions from all comers.

Making up the remainder of the Scientific Assembly at San Francisco were hundreds of general and specialty lectures, dozens of motion pictures, and eight color telecasts.

Programs for both the Annual and Clinical meetings are under the direction of the A.M.A. Council on Scientific Assembly. Secretaries of the sectional specialties develop their own programs for the Annual Meeting with the aid of the Council. A new program approach to be tried at the Annual Meeting next summer will be the combining of several sections to provide an across-the-board view of a single theme. Proposed topics: childbirth and liver disease. For the Clinical session, designed more for the general practitioner, the county society of the area in which the meeting is held plans the three-day session with the Council.

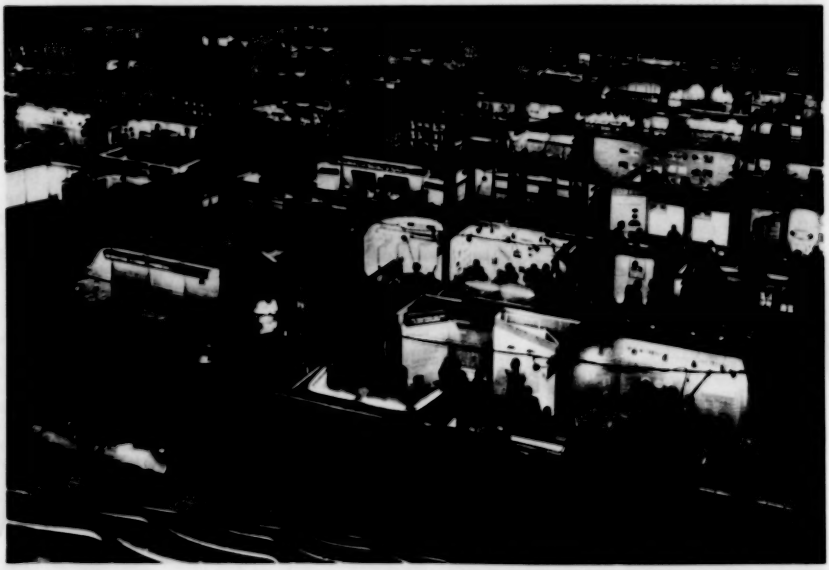
Show on the Road

Preparing for an Annual Meeting (and to a lesser extent a Clinical session) is not a simple task. Coordinated by Thomas Hull, Ph.D., Secretary of the Council, and aided by George Larson, Manager of Covention Services, it is nearly a self-sufficient unit.

"We are prepared to move into four walls and a roof and stage the Scientific Assembly," Larson says. He packs everything from a special wide chalk (so blackboard marks can be read from the last row) to slide projectors (in two sizes to accommodate differing transparencies). In addition, he totes along lap boards, flashlights, easels, movie projectors, lecterns, aisle lights, transparency cases, movie screens, and dozen of other items.

There is no record of the size of the Baltimore meeting room which housed the first Annual Meeting of the A.M.A., but it probably did not need to hold more than 300. So complex have housing arrangements grown in the intervening century that today only three American cities—New York, Miami Beach, and Atlantic City—can comfortably house the Annual Meeting.

More than 13,000 member physicians descended



Glowing like a city in miniature, aisle after aisle of scientific exhibits await the visiting physicians just before the opening of last summer's Scientific Assembly in San Francisco. Viewed from the convention hall's balcony (note figures seated at lower left), the lighted display offers an indication of the scope of medicine's most popular "postgraduate course."

on San Francisco for the 1958 session in June. The largest meeting ever held was in New York City in 1957, and it pulled 19,469. Convention statisticians say each physician can be counted on to attract 3.5 other persons: nurses, guests, medical students, technicians, interns, and residents. Figures show that nearly 45,000 persons were drawn to the Golden Gate City for this year's Annual Meeting.

Education on His Mind

Unlike many convention-goers, the physician headed for his Annual Meeting has education uppermost in his mind. He seeks new facets of knowledge and a new look at those areas familiar to him. How does he view this semi-annual effort? Generally, he's pleased, although he sometimes finds fault with some of the physical facilities or with the emphasis placed on certain portions of the program.

In surveys conducted among doctors who participated in two of these scientific sessions, the following comments were typical:

—"The entire meeting was worth as much as a two-week postgraduate course."

—"An excellent meeting. My only trouble was that I could not be in two places at the same time. . . . I'll be back next year."

—"There should be greater emphasis on psychosomatic medicine, emotional disturbances, and personality disorders."

—"At least 50% of all presentations should be left out to devote more time and intimate handling of subjects of importance to the greatest number attending."

The Clinical session due next month in Minneapolis will attract fewer guests than the Annual Meeting but will be of a similar type. Instead of 300 scientific exhibits, there may be 90. Instead of staying five days, many of the guests will remain for three.

Five Year Plan

But to Dr. Hull or George Larson plans for the Minneapolis meeting are now almost a thing of the past. They finished with that one (except for the execution phase) long ago and are now hip-deep in plans for Atlantic City next June. Even next summer's affair is well under control (the Council met with the section secretaries last month), and eyes are on more distant fields.

The A. M. A. is scheduled to be in Dallas next winter, and in Miami Beach in the summer of '60. After that comes Washington and then New York City again.

New York, Atlantic City, and Miami Beach are the only places with facilities that really fit the needs of the A.M.A's largest gatherings. These needs include a giant-sized exhibition hall, 14 meeting rooms (with ceilings high enough for motion pictures) with seating for as few as 200 and also for as many as 2,500, and lots and lots of hotel rooms. These facilities should be grouped conveniently to cut down on inter-meeting traffic problems.

Chicago, although it prides itself on being a convention town, has trouble furnishing the meeting space the A.M.A. would like. San Francisco, on the other hand, lacks hotel rooms, a factor officials say probably cut attendance last year.

But wherever they're held, A.M.A. meetings lead the list of human gatherings. After it was all over in San Francisco last June, Walter Swanson, the city's convention manager, called the A.M.A. influx "the largest mass migration of humanity in modern times outside the military."

Dr. Alphonse McMahon of St. Louis is Chairman of the Council on Scientific Assembly. Other members are Drs. J. Arnold Bargen of Rochester, Minn.; Michael E. De Bakey of Houston; L. W. Larson of Bismarck, N. D.; Carl A. Lincke of Carrollton, Ohio; Samuel P. Newman of Denver; Stanley P. Reimann of Philadelphia; Walter Scott of Los Angeles; and Henry R. Viets of Brookline, Mass. Thomas G. Hull, Ph.D., is Staff Secretary.

Doctors Spark Health Survey

A thorough study of all phases of indigent medical care is under way now in Florida, due largely to the efforts of the Florida Medical Association. Aimed at blueprinting future needs and services for medically indigent, the year-long project was launched this summer by Governor LeRoy Collins, who appointed a Citizen's Medical Committee on Health chaired by Dr. Edward R. Annis of Miami.

It was the state medical association, backed by other groups and individuals, which urged creation of the committee to study particularly outpatient services and care of the chronically ill. The committee also will make recommendations relating to maximum utilization of state health services, the role of voluntary agencies, and utilization of trained personnel.

Research by individual survey teams will complement data from state bureaus. This technique of study will examine population trends, hospitalization data, nursing homes, distinctive health and medical problems of the aged, and the possibilities of insurance for the aged and chronically ill.

A. M. A. Council Meets with Ten 'Third Party' Medical Chiefs

I propose that the medical profession and third party payers engage in a cooperative project for the delineation of criteria by which the quality, economy and improvement of medical care can be measured and judged with a fair degree of accuracy.

That statement sums up the viewpoint expressed by Dr. Warren F. Draper last month (October 17) at a meeting of the A. M. A. Council on Medical Service with medical directors of ten medical programs, most of them sponsored directly or indirectly by labor groups. (See Organization Section, THE JOURNAL, Sept. 20, 1958). Dr. Draper is executive medical officer of the United Mine Workers of America Welfare and Retirement Fund.

It was the first such conference called by the Council in its efforts to clarify third party relationships. Participants noted that the six-hour session in Chicago was marked by an air of cordiality combined with frank discussion. Later this month, according to Chairman Joseph D. McCarthy of Omaha, the Council will meet similarly with representatives of Blue Shield and Blue Cross. Next month, plans call for conferring with private insurance company officials, and also with representatives of management. Early in 1959 there will be a Council session with government representatives. "Eventually, we expect that all of these third parties may be brought together by the Council in a national conference," Dr. McCarthy said.

Following are selected comments from physicians invited to the October 17 meeting:

Herbert K. Abrams, Union Health Service Inc. of Chicago—"When any new health plan arises, the physicians who are not in it are against it—until they realize it is here to stay as it grows and matures. That is the experience of history. . . . The emphasis of our service is preventive care. Physicians have complete control over all medical care rendered. We confer frequently with the Chicago Medical Society, and all of our physicians must be medical society members . . . The A. M. A. Guides for Evaluation of Management and Union Health Centers are correct when they state that health centers 'should be allowed to prove or disprove their merit, so long as they provide care of high quality.'"

David Barr, Health Insurance Plan of Greater New York—"Our relationships with local medical societies are not deteriorating. However, these societies act and think friendly at informal meetings only. They do not follow through at their meetings of delegates when official policy is made. . . . This meeting today is very encouraging."

Cyril Costello, Medical Institute of Meat Cutters' Local 88, St. Louis—"Our program allows free choice of physician and hospital. Physicians, all of whom are part-time with the institute, must be local medical society members, must be faculty members of at least one of the two university medical schools in the St. Louis area, must be in private practice, must be board-certified in their specialty and must be a private hospital staff member. Soon we will begin a program to emphasize preventive aspects to an even greater degree than exists now."

Cecil Cutting, Permanente Medical Group—"It is a firm policy to urge the Health and Welfare Fund to offer employees a choice of joining the direct service group practice prepayment plan (Kaiser Foundation Health Plan) or joining a fee-for-service type of plan like Blue Shield, Blue Cross, or that offered by private insurance firms. . . . Qualified physicians who are not in the Permanente Medical Group, on application, are granted courtesy staff privileges at Kaiser Foundation Hospitals, which are accredited by the Joint Commission. . . . The evolution of different forms of medical care organization and different forms of prepaid medical care to meet the needs of the people is both a natural and healthy development in our free, private enterprise economy."

Warren F. Draper—"Liaison is out of the question where medical societies engage in programs of harassment against us. Yet, relationships with medical societies are improving. In West Virginia and some other states we get along well. Still, so many physicians do not know the true facts—and as a result they make the wildest statements. Satisfactory principles and good relationships between organized medicine and paying agencies can be accomplished only through the development and utilization of accurate information in place of the dubious expressions of opinion which have formed so large a part of resolutions of medical societies at every level in recent years. . . . When this health program was started I was convinced it was a unique situation peculiar to the UMWA. Now I've learned a lot—that other people, splendid people associated with other programs—have the same basic problem. We all have to work it out together. . . . Things are not so black."

Henry H. Lichtenberg, Group Health Association of Washington, D. C.—"Our patients wanted to delegate their choice of physician to others rather than accept it themselves. The plan also gave us physicians reasonable security of income and hours. . . . There are good relations with the local medical society and several of us are active in it."

Frederick D. Mott, Community Health Association, Detroit—"We expect to announce a program in the next 12 months. It will be a community-based

Chairman of the Council on Medical Service is Dr. Joseph D. McCarthy of Omaha. Other members are Drs. J. Lafe Ludwig of Los Angeles; Russell B. Roth of Erie, Pa.; H. B. Wolley of Idaho Falls, Idaho; Carlton E. Wertz of Buffalo; T. J. Danaher of Torrington, Conn.; Robert L. Novy of Detroit; R. B. Chrisman Jr. of Coral Gables, Fla.; John F. Burton of Oklahoma City, and David B. Allman of Atlantic City. Staff secretary is Mr. George W. Cooley.

program gaining counsel, not only from the United Auto Workers, but from many walks of life—the clergy, bankers, and others. It will be a health program—not just sickness insurance—with emphasis on prevention and rehabilitation. We will make certain that individual members be able to have a choice of service. We urge a personal physician relationship. All medical matters are to be in medical hands—no lay domination. . . . We are anxious to develop our program in the framework of organized medicine. If we do build hospitals, they will be open to all physicians and all patients. . . . There are many physicians devoting their lives to direct service—good men—and organized medicine will be the loser if these men are pushed aside and kept out of the house of medicine."

Leo Price, International Ladies Garment Workers Union Health Center, New York City—"Our emphasis is on preventive aspects. Service is restricted to the ambulatory level and hospital assistance—not comprehensive care—because there is lack of funds. . . . It seems to me that the challenge of this broad problem is to communicate the great work of the A. M. A. to local groups."

William A. Sawyer, consultant, International Association of Machinists, Rochester, N. Y.—"We stress preventive care. . . . I am also reporting on a projected health care plan in Rochester, a joint management-labor effort for clothing workers. It is being taken up with the local medical society now."

George Shucker, Sidney Hillman Medical Center, Philadelphia—"We want to emphasize the preventive aspect of our program because to our knowledge there is no prepaid or non-profit insurance agency that sells unrestricted ambulatory preventive care. . . . Our pattern is to seek and get county medical society approval before setting up a center. . . . We need more meetings such as these—not only with the medical directors but also with administrators of our plans."

Societies Getting Part of Medical Care Plans Report

After many months of conference and study, distribution of Part 2 of the final report of the A. M. A. Commission on Medical Care Plans will be made next week (beginning Nov. 10) to all county and state medical societies. Part 2, which consists of statistical appendices and background material, was approved by the House of Delegates last June. The seven appendices consist of:

—Characteristics of 107 miscellaneous and unclassified plans surveyed by mail questionnaire.

—A directory of 246 plans for which information was available to the Commission.

—Results of several surveys on provisions and characteristics of medical society approved prepayment plans, including Blue Shield, and group and nongroup private insurance programs.

—Results of surveys on nonoccupational medical care and occupational disability programs in industry.

—Selected statutory provisions of workmen's compensation laws.

—Information on monetary aspects of workmen's compensation.

—Selected Judicial Council opinions and House of Delegates policy statements which were considered pertinent to the Commission's inquiry.

The Commission's study attempted to determine, among other matters:

1. The nature and methods of operation of the various types of plans through which persons receive the services of physicians.

2. The effect of these plans on the quality and quantity of medical care provided.

3. The legal and ethical status of arrangements used by the various plans.

Part 1 of the final report of the Committee on Medical Care Plans, with findings and recommendations, has been completed and submitted to the Board of Trustees for review and appropriate action.

Members of the Commission on Medical Care Plans are Drs. Leonard W. Larson of Bismarck, N. D., Chairman; David B. Allman of Atlantic City; H. Russell Brown of Watertown, S. D.; John F. Conway of Clovis, N. Mex.; F. J. Elias of Duluth, Minn.; Percy E. Hopkins of Chicago; H. Gordon MacLean of Oakland, Calif.; J. D. McCarthy of Omaha; Homer L. Pearson of Miami; Leo Price of New York; James R. Reuling of Windermere, Fla.; William P. Shepard of New York; Norman A. Welch of Boston; Mr. E. J. Faulkner of Lincoln, Neb., and Mr. Jay C. Ketchum of Detroit.

Compile List of Group Practices

The significance of group practices as an arrangement through which physicians provide medical care is illustrated by a roster of group units being compiled by the A. M. A. Council on Medical Service.

The Council recently mailed a verification sheet to 1,008 groups listed in a card file compiled from membership rosters of the American Association of Medical Clinics and the National Association of Clinic Managers, and from news clippings and letterheads.

A breakdown of 822 replies from groups in the U. S., Hawaii, and Canada shows 8,958 physicians practicing in these groups. While 100 of the groups answering had only two physicians, 689 included more than two. The mailing showed 18 groups had been dissolved and 15 former two-man groups had been split into individual practices.

Physicians in group practice not yet contacted are asked to send the following information to the Council: group name, address, offices (rented or owned), number of physicians, and specialities.

Purpose of compiling the information is the publication, in a few months, of a directory of group practice units.

Expansion of Rehabilitation Units Sought in State Societies

Last spring, the A. M. A. Committee on Rehabilitation polled constituent member societies to learn whether they had committees on rehabilitation. It now finds that, of the 49 responding, 25 have such units but that "all too frequently, the Committees' activities are limited to some form of liaison or cooperation with the state's Office of Vocational Rehabilitation."

Meeting in Chicago Sept. 27, the A. M. A. Committee discussed methods of encouraging the formation of rehabilitation committees by state societies that do not now have them—and urging those that do to expand their activities.

Those discussions, not yet formalized, centered on the following possible objectives:

—Coordinate rehabilitation interests and activities within the society.

—Foster medical supervision of rehabilitation services and centers.

—Study the problems and relationships of medical, social, educational and vocational aspects of rehabilitation (see Medicine at Work, THE JOURNAL, Nov. 2, 1957).

—Inform the medical profession on the availability of rehabilitation services.

—Collect information on the establishment, operation and utilization of rehabilitation services.

—Encourage county society interest in and programs on rehabilitation.

Implementing a wide-spread concern of organized medicine with the challenge of rehabilitation, the two year old Committee on Rehabilitation is made up of one representative each from the A. M. A. Councils on Medical Service, Medical Physics, Mental Health, Industrial Health, and Medical Education and Hospitals.

Community Rehabilitation Services More Practical Than a Center

While it is important to treat "the whole man" in any effort at rehabilitation, it may be unrealistic to require that his medical, psychological, social, and vocational needs be all taken care of under one roof.

That was the conclusion reached by two A. M. A. Committees when they met jointly in Chicago Sept. 27 to discuss the practical effect of the Hill-Burton law restrictions on construction of rehabilitation facilities.

Dr. Willard A. Wright, Chairman of the Committee on Medical and Related Facilities, said his Committee's recent study of the practical applications of the Hill-Burton law showed that more emphasis was needed on rehabilitation facilities. He pointed out, however, that the present wording of the law makes it difficult for small hospitals to take part in that part of the program because it requires them to provide a rehabilitation facility which includes medical, psychological, social, and vocational services.

Noting that only 62 centers had been built with Hill-Burton aid since the category was added in 1954, Dr. Edward C. Rosenow Jr., a member of Wright's Committee, said: "That's not many for the entire United States."

Dr. Frank H. Krusen, Chairman of the Committee on Rehabilitation, said his group felt it was important to provide all rehabilitation services within the community but that these need not necessarily be within the hospital itself if to do so would be a great burden.

D. C. Rehabilitation Study Links Medicine with Other Groups

"A study [of rehabilitation] would not be complete without the opinion of the practicing physician."

Putting action to those words, the Council on Rehabilitation recently began a survey of doctors in Washington, D. C.'s metropolitan area as a part of its broad study of rehabilitation services. The Council is sponsored by the medical societies of the District of Columbia, the city of Alexandria, the Virginia counties of Arlington and Fairfax, and the Maryland counties of Montgomery and Prince Georges.

Supported in part by a grant from the federal Office of Vocational Rehabilitation, the project was begun in mid-1956 "to study existing rehabilitation facilities and to assess present and future needs." Another aim of the study is to demonstrate the role

Handy 'Handicapped'

The slogan says: "Hire the handicapped—it's good business."

E. I. duPont de Nemours and Company of Wilmington, Del., agrees that it is and has the figures to prove it. "An overwhelming majority of the more than 1,000 physically handicapped employes of the Du Pont Company have achieved average-or-better levels of job performance, safety, and attendance," the firm's Employe Relations department said recently. It based its conclusions on a study made last summer in the company's plants, laboratories, and offices.

So severe is the company's definition of what constitutes a handicap that "many employes who normally would be considered handicapped were not included in this study," an official said. Not only that, but some of Du Pont's best performers have the most severe handicaps—amputation, blindness, deafness and paraplegia.

of the local medical society in total rehabilitation planning.

The need for cooperative effort in such a project is underlined in an interim report reviewed last month by the A. M. A. Committee on Rehabilitation. The report said: "There is a growing recognition that problems do not confine themselves to jurisdictional boundaries." One of the early conclusions reached by the Council was that the physician's role in the rehabilitation partnership should be given even more emphasis than originally thought.

Chairman of the Committee on Rehabilitation is Dr. Frank H. Krusen of Rochester, Minn. Other members are Drs. Walter H. Baer of Peoria; Guy A. Caldwell of New Orleans; Oscar A. Sander of Milwaukee; and Hoyt B. Woolley of Idaho Falls, Idaho. Dr. Ralph E. De Forest is staff secretary.

Symposium Explores Medicine's Vertical Frontier

What special kind of nutritional problems must be considered in planning an interplanetary voyage? That and other questions related to the well-being of man in space are being explored this coming week in a worldwide exchange of information and ideas at San Antonio, Texas.

The Second International Symposium on the Physics and Medicine of the Atmosphere and Space on Nov. 10 through 12 will emphasize man's adaptation to space conditions, including an altered concept of time. Other specific problems scheduled for discussion involve medical and psychological aspects of launching and re-entry.

Keynoting the symposium will be an address by Major Gen. Otis O. Benson Jr. on "Common Platform of Physics and Medicine in the Advance of the Vertical Frontier." Dr. Benson is Commandant of the School of Aviation Medicine at Randolph Air Force Base, where recent studies have shown that practical space travel for humans is in the near future (see Medicine At Work, THE JOURNAL, June 15, 1957). He is scheduled to introduce Lyndon Johnson, Senate Majority Leader, as dinner speaker.

Among more than 50 civilian and armed forces scientists scheduled to make presentations at the symposium are the Air Force Chief of Staff, Gen. Thomas D. White; Air Force Surgeon General Dan C. Ogle; Dr. Hubertus Strughold, Professor of Space Medicine at the Air Force School of Aviation Medicine; Dr. Werner von Braun, technical director of the Army Ballistics Missile Agency, and Col. John Paul Stapp, chief of the Air Medical Laboratory. The conference, sponsored by the School of Aviation Medicine, is being conducted by the Southwest Research Institute.

'Lifelong Study' Is Keynote of Medical Education Conference

When does a physician stop studying medicine? Never.

Announcing the theme, "Medicine—A Lifelong Study," trilingual invitations to attend the Second World Conference on Medical Education have been mailed to physicians and other members of the health professions in the U. S. and more than 60 foreign countries. The five-day conference will open on Aug. 30, 1959, at the Palmer House in Chicago under the auspices of the World Medical Association. Collaborating in the presentations are the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities.

According to the provisional program, there will be three days of section meetings between the opening and closing plenary sessions. These sections will be concerned with basic clinical training for all doctors, advanced education for general and specialty practice, the development of teachers and investigators, and continuing medical education. The theme topic will be carried in a presidential address by Dr. Raymond B. Allen, Chancellor of the University of California in Los Angeles. Other major presentations will consider international cooperation in postgraduate education, and the value of participation in research as a component in the education of physicians.

Arrangements are being made for participants to join three afternoon tours of medical schools and hospitals in Chicago and to visit A. M. A. headquarters. At the conference scene there will be technical, medical film, and audiovisual aids exhibits. During sessions, simultaneous translation will be provided in English, French, and Spanish. Governments, medical schools, and national and international bodies concerned with medical education will be represented at the conference.

(Any person who is interested in medical education may apply for conference registration by communicating with Dr. Louis H. Bauer, secretary general of the W. M. A., at 10 Columbus Circle, New York 19.)

Founded 11 years ago, the W. M. A. is a nongovernmental confederation of 53 national medical associations representing a total membership of more than 700,000 physicians. As "the international voice of medicine" (see Medicine At Work, THE JOURNAL, Sept. 7, 1957), it has been promoting research, sounding the alarm when physicians and their patients have been oppressed, and reporting on the activities of at least 23 other international organizations as they affect the practice of medicine.

Picture of Medical Education Coming in Next Week's JOURNAL

One of the broadest, and yet most concise, pictures of medical education in the U. S. and Canada will be seen in next week's issue of THE JOURNAL. More pictorial than ever before (with scenes from at least a dozen schools), the educational issue includes material on virtually every phase of medical education during the 1957-1958 academic year. Following is a preview sampling of some of that highly significant data:

Enrollments—A new record high for the ninth year, 8,030 entering students. Four schools—Tennessee, Michigan, Jefferson, and Illinois—each with four-year enrollments of over 600. The average prospective medical student applied to four schools to gain admission—60,946 applications filed by 15,791 applicants. Over 20 times as many U. S. citizens enrolled in Canadian medical schools as Canadians enrolling in the U. S., but the exact figures (82 and 4) are quite low. One out of every 18 medical school enrollees in the U. S. was a woman (total 1,644); approximately the same proportion of graduates was female, although in four schools (Howard, Boston University, Wayne State, and Western Reserve) the graduating percentage of women was 10% or more. Of course, Women's Medical College enrolls no men.

Financing—"Less than one per cent of the nation's bill for medical care is being spent for medical education," writes Mr. A. J. Carroll, Business Officer of the State University of New York, in a criticism of "inadequate financial reports" from medical schools. He adds: "Educators, doctors, students, health personnel, legislators, government officials, university officials and the general public—all are confused about medical education, what it costs, what it means to them, what they are paying for it, and what they should be paying." But there may be clarity soon, Carroll states, as the result of a recent grant from the W. K. Kellogg Foundation to underwrite a study of medical school financing—"this study for the first time will be able to prove the financial needs of medical education, and to establish new standards of management efficiency."

Progress and Experimentation—Forty-nine of the 85 operating medical schools in the U. S. and 7 of the 12 Canadian schools reported major new developments. These include a plan at Duke University to prepare physicians who are also skilled medical research scientists; a greater emphasis on educational methods for medical teachers at the University of Buffalo; the first report on a 12-year evaluation study of the medical education program at Western Reserve; studies of the sociology of medical education conducted at Cornell, Western Reserve, and the University of Pennsylvania; and an experimental program at the University of Pittsburgh whereby medical students whose separate career-hopes lie toward research, clinical specialties, and general practice might adapt their education flexibly to reach any of those three objectives.

Two New Committees Ready for Studies on Insurance, Radiation

The A. M. A.'s two newest Committees—one whose mission is primarily socioeconomic, the other basically scientific, but both concerned with major influences in modern times—are ready to begin their separate studies.

The nine-man Committee on Insurance and Prepayment Plans, under the Council on Medical Service, held its first meeting late in September and will meet again in early January. It is considering matters relating to insurance written by private companies and by Blue Shield and Blue Cross and to prepayment health care plans.

The nine-man *ad hoc* Committee on Atomic Medicine and Ionizing Radiation, under the Council on Medical Physics, is expected to meet for the first time within a few weeks with two main objectives:

1. Identify the broad problem of ionizing radiation as it pertains to the health and medical needs of the public—including the hazards, effects, prevention and treatment of radiation exposure to mankind and the environment.

2. List the areas requiring attention in a suggested order of priority.

Less than one dollar out of five spent for medical education is contributed by the student, the American Medical Education Foundation reported this month as its annual fund drive gained headway. Formed by the A. M. A. in 1951 to aid medical schools with their financial problems, the foundation has given more than 7 million dollars to medical education in the seven intervening years.

John W. Hedback, executive secretary of the A.M.E.F., said: "Contributions come chiefly from doctors and their wives, both individually and through state and county societies. About half the money has been sent to schools specified by the donors. The other half has been divided equally among the schools."

Vol. 168, No. 10

The Troubled Employee

He Looms Large As an Economic Loss, Community Problem, Medical Challenge

Milton Golin

In one day several years ago, five employees of a large East Coast industrial firm went to supervisors to complain about their jobs: Schedules were too difficult. Co-workers were intolerable. Office equipment was no good. Other departments were uncooperative. There was too much noise—or glare—or heat—or cold. Because they also complained of backache, headache, and abdominal pain, they were referred to the plant medical office. There, a company physician who happened to be a psychiatrist listened to their gripes and relieved their hurts. He also found that only one complaint could be traced to actual work conditions. These were the true causes of the other four:

A stenographer whose boy friend had stalled her for a long time had become panicky at the thought of losing him.

An account executive was afraid he would inherit the heart disease that killed his father, and the paranoid tendencies showing in his mother.

A young salesman was ashamed that he could not make up his mind about two girls who were in love with him.

A foreman was sick with the feeling that he was to blame for his wife's depression, which led her to threaten the lives of their two children.

How much business did the salesman lose that day? What major blunder crept into the steno's work? Where did the account executive fail to make an important decision? How many workers reacted in what way to the mood of their guilt-laden foreman? These may be questions for the economist, the sociologist, the administrator. But they also are questions for the family doctor. The troubles of these four employees, as of thousands more weighed down with anxieties, concern the entire medical profession because both personal and public health are at stake on a nation-wide scale.

The American Medical Association, mindful of the many-sided problem, this year established a Joint Committee on Mental Health in Industry—made up of members and designates of the Councils on Mental Health and Industrial Health—to explore the field. All five Committee members this month are beginning their study on the premise that industry is not an island of people at work. They know that industry is part of the human community and that it is another of man's several social units. For in industry, perhaps more than in any other area of American life, we are constantly being reminded of the dissatisfactions, strife, and violence that occur among people.

There is little doubt that, by and large, these people are sufficiently attuned to their jobs so that work and private problems hardly ever come into serious conflict. At the same time, industry has its severely troubled but otherwise normal employees: The homely typist without companions. The corporation lawyer who endures his distasteful job for security though he really longs to be an artist. The machinist whose wife's illness makes him do double duty as provider and homemaker for his children. The girl on the assembly line whose home life is disrupted by an alcoholic father.

That kind of unhappy or worried employee is the "accident prone" who unmeaningly violates the safety rules and suffers one mishap after another. He is the goldbricker, the trouble-maker, the one who will lose his job and cost perhaps thousands of dollars to replace. He has the ability but not the attitude to hold his job. A psychiatrist who is making a career out of the study of mental health problems in industry, Dr. William C. Menninger, says: "From 60 to 80% of all dismissals in industry are due to social incompetence and only about 20 to 40% to technical incompetence. What may be more important, we know that one emotionally disturbed employee can mess up his whole department like the proverbial single rotten apple in the barrel, and that the cost of such a person can hardly be estimated."

There are guide lines for gauging the cost, however. In one General Motors Corporation plant of

Members of the A. M. A. Joint Committee on Mental Health in Industry are Drs. Leo H. Bartemeier of Baltimore; Leonard E. Himler of Ann Arbor, Mich.; Charles F. Shook of Toledo; W. Donald Ross of Cincinnati; and Ralph T. Collins of Rochester, N. Y., chairman. Staff secretary is Dr. B. Dixon Holland.

5,800 employees, psychiatric and psychological problems were found in more than half of the workers reporting for medical care; most actually were made physically ill by those emotional problems. California's industrial accident commission announced that in one year the state paid out 15 million dollars to compensate employees suffering from some kind of neurosis associated with an in-plant injury. According to a Chicago Association of Commerce and Industry publication, maladjusted workers cost U. S. industry at least 3 billion dollars a year through repeated job changes, alcoholism, vandalism, prolonged work absence, executive breakdowns, and other signs of mental and emotional difficulties.

One corporation sent its best technician-executive on a three-months' tour of Europe with an important mission. The man failed miserably. Only much later was it learned that his wife was mentally ill and that he was worried about her and about conditions at home all the time he was away. His wife's illness was an enormous liability to the company, which might have saved itself expense, and saved the executive anguish, if a physician had picked up hints of the difficulty in a periodic examination or in day-to-day contacts with the man.

Who Are the Helpers?

Doctors employed in industry have many allies, both within and outside the profession, to help them detect such danger signs. Foremost, of course, is the family physician. As health advisor he, more than anyone else, is in a position to do a preventive job by minimizing the effects of his patients' personal problems. This should make the general practitioner a key man for maintaining mental health in industry. Other key figures are industrial nurses, supervisors, personnel officials, counsellors—and psychiatrists. Unfortunately, although most companies accept all of these individuals as essential contributors to mental health in industry—a surprisingly large number hesitate to employ the one most concerned—the psychiatrist—on a full-time basis. One corporation president commented: "Sure, psychiatrists are all right, but if we have one on the regular payroll, people will wonder what's different about our employees."

In all of the United States there are only a half dozen companies which employ full-time industrial psychiatrists. These include Du Pont, International Business Machines, American Cyanamid, America Fore Insurance Group, and Metropolitan Life. However, at scores of other firms—such as Caterpillar Tractor, Kraft Foods, American Telephone and Telegraph, and the Detroit automakers—psychiatrists work part time or on a consultant basis. According to a survey made this summer by the *Wall Street Journal* (which calls mental illness "industry's top medical problem") company psychiatrists seldom give long-term treatment. Dr. Alan A. McLean, full-time psychiatrist at IBM, said: "We're not here to compete with private practicing physicians. Our job is to diagnose emotional disorders and determine whether they should be referred for psychotherapy."

Industrial nurses play a vital role in mental health. One alert nurse in a Western Massachusetts metal-working concern several years ago wondered why a craftsman showed up twice within a short period for treatment of finger injuries caused by careless handling of his machine. She drew him out and learned that he was worried about where to turn for aid for his wife, pregnant at middle age. The nurse simply told him where to find a social agency that could help his wife. No psychiatrist, she nevertheless provided the kind of counselling that nurses, personnel men, foremen, and others may develop under the guidance of a psychiatrist or other physician. The guidance must be proper, of course, for misguidance may easily do much more harm than good.

Pioneering Study

An example of proper guidance is in the Western Electric Company, whose Hawthorne Works in Cicero, Ill., 32 years ago became the laboratory for a pioneering study which has not yet been equalled in thoroughness and intensity. The study was intended to find out what kind of lighting would help boost production. But the plotting of one "average output" curve led to another until, before long, research was going on full blast into what makes a worker tick. The researchers found that better lighting increased output, all right, but that reduced lighting also increased production. Why?

That five-year experiment demonstrated that by merely exhibiting interest in workers—as each re-

The Desk Set—One Man's Worry

Officials of an East Coast business firm were puzzled over the change in one of their executives after he was transferred to another job in the plant. He was receiving the same salary and he had equal responsibilities, but, despite assurances that it was a lateral shift only, the man developed all the symptoms of acute anxiety. He lost sleep, his appetite fell off, and he could not concentrate on his work. By chance, Professor F. J. Roethlisberger of the Harvard University School of Business Administration happened to be conducting a study of that company. He recognized that an unofficial symbol of status there was possession of a twin pedestal desk. The executive had been transferred to a desk with only one pedestal. At Roethlisberger's suggestion, the man was given a two-pedestal desk and his symptoms disappeared almost immediately.

Vol. 168, No. 10

New Problems, New Needs

The business community must bear at least some of the responsibility for creating mental health problems of its employees, according to *Business Week*. An article in that national magazine states: "Executives fail to realize that they themselves are partly responsible for changes that have raised new worker problems. . . . Fifty years ago a man followed his father's footsteps, used his hands to produce a finished product and he could take satisfaction in his handiwork. Today the worker is separate from the finished product. He is not able to feel the same satisfaction in seeing a job well done." The article also states, "The big problem for industry is finding the right doctor. Specifications are exacting. He has to know his medicine and he has to be a good listener when it comes to sob stories. He has to be an intermediate between worker and management without looking like a company spy. In short, he has to be a combination of Dr. Christian of the movies and an army chaplain."

searcher did—management was able to make them happier and more productive. It did not take long for the company to realize that a counselling program would sustain that interest. Several score Western Electric counsellors, skilled listeners who were always present, encouraged the worker to talk about anything at all—never interrupting, never arguing, never giving advice. Often the result, according to the company, was that employees seemed to talk their troubles away, re-examined their thinking in the sound of their own words, and acquired a social skill in relationships with fellow employees.

An echoing comment comes from Dr. Leo Wade, medical director for the Esso Standard Oil Company, who says: "Many times a worker will come in with a complaint and all he needs is a sympathetic ear. After he talks to us awhile and gets his trouble off his chest, he begins to feel better."

Western Electric cites a good example of this, an employee of 20 years' experience who began hitting the skids until he was doing the lowest grade of work in his department. He became so edgy that no one dared approach him for fear of triggering an accident at his machine. His locker was a small drugstore of medicines. He complained that even when his back was turned he could feel the foreman's eyes boring through him—always spying on him. Company counsellors uncovered an extreme case of social isolation. The man lived alone, locked himself in his room each evening, dosed himself with whisky and medicines, had no friends, and rarely visited his only relative.

After three weeks of skillful interviewing under medical supervision, nothing more than what might be called friendly chats, the employee's fears faded away. His work improved, he began to take an interest in co-workers, and his rise again to a responsible position of leadership became a matter of course.

Importance of Leadership

Of all factors that influence mental health in the office and factory, the foremost is leadership. The special pressures on many an executive—frustrations, fear of failure and feeling of insecurity—inevitably will either warp or stabilize the attitudes of people under his leadership, depending upon his own approach in handling those pressures. "That is why the executive's well-being is of vital concern, not only to himself but, even more importantly, to those he leads," says Dr. Ralph T. Collins of Rochester, N. Y., Chairman of the new A. M. A. Joint Committee on Mental Health in Industry, and neurological and psychiatric consultant for the Eastman Kodak company. "There are cases of companies which reached the brink of bankruptcy because they had emotionally sick men at the helm—men particularly difficult to treat because of their position. There are supervisors who are autocratic and domineering, who are unable to make a decision or to delegate responsibility, who are bad-tempered, who are unreasonable, who are unable to win respect.

"Fortunately, this kind of executive is in the minority for the very reason that our economy places such a high premium on production; he is less likely to survive in competition with the executive who

does gain the respect and added effort of his workers."

That is only part of the reason, however, and it may even be the wrong part. For the core of our mental health problem in industry, according to Dr. Menninger, is "a mixing of our values system. We tend to focus on and hear about one side of industry, which has as its chief goals the increase of production and the increase of profits. But money won't bring or buy the loyalty or high morale we strive toward. So much of job satisfaction depends on the personal values that are gained in human relationships through mutual respect and dignity, confidence and belonging and, yes, love."

The Problems

That concept indicates that, while management generally may be aware of its deep involvement in the worker's personal problems, it also needs medical guidance in dealing with employees so that emotional difficulties will not be created or aggravated. Says Dr. Collins of the A. M. A. Committee: "Meeting that need represents the biggest task of the physician—whether he is a full-time industrial psychiatrist, one of the 5,000 doctors who devote their careers to the broad field of occupational health, or one of the 20,000 other physicians who serve industry part time or on call (see Medicine At Work, THE JOURNAL, March 30, 1957). The doctor employed in industry can work two different ways to preserve mental health. He can see that the worker gets emotional first aid in the form of brief psychotherapy after early diagnosis, and he can emphasize preventive aspects in his role as consultant in labor and industrial relations."

What Is Being Done

Actually, this is what many physicians, in cooperation with management and labor, are doing to brighten the mental health picture in factories and offices—and, thereby, in communities—across the land. These are other current developments pointing toward progress in this expanding field:

—This month, on Nov. 20, the A. M. A. Joint Committee on Mental Health in Industry will meet in Chicago for the first time to plan its program.

—Since last February, under the auspices of the American Management Association, top executives from scores of business firms have been gathering at Saranac Lake, N. Y., for concentrated sessions on human factors in industry. The courses are conducted by psychiatrists (like Dr. Collins) and other authorities in the field.

—Three weeks ago the New Jersey Industrial Health Conference devoted half of its day-long program to emotional factors in the work environment.

—More and more state and local medical groups are establishing committees on mental health in industry.

—The World Health Organization this year is launching a study of the effects of automation on mental health.

—This year, for the first time, the Industrial Medical Association created a committee on mental health in industry.

—Work is being completed now on the first phase of a massive study of human relations in industry. The project, begun three years ago and financed partly by a grant of the Rockefeller Foundation, is being conducted by the Menninger Foundation's clinical staff. In order to gauge the measure of corporate actions upon workers' mental health, researchers so far have conducted "in-depth" interviews of more than half of the 1,900 employees of the sprawling Kansas Power and Light Company. Using this study as a base, the Menninger Foundation hopes to develop a program having far-reaching effects on mental health in industry.

Promise of the Future

Those developments point toward the solution of a host of complex problems evolving out of our expanding industrial society. But what kind of

Foremen rate "good wages" as the most important condition of their jobs, but the men who work under them believe that appreciation for good work is most important—according to results of a survey reported by the Labor Relations Institute of New York. The Institute prepared the following chart to show how both groups feel on this point:

JOB CONDITIONS	WORKER RATING	FOREMAN RATING
Appreciation for good work	1	8
Feeling "in" on things	2	10
Help with personal problems	3	9
Job security	4	2
Good wages	5	1
"Work that keeps you interested"	6	5
Possibilities for promotion	7	3
Personal loyalty to the workers	8	6
Good working conditions	9	4
Tactful discipline	10	7

program can be formulated to prevent these problems from arising in the future?

—Already, there are mounting efforts by leading psychiatrists to instill upon top management officials the idea that there should be greater emphasis on "capacity for human understanding" in the rating and selection of executives. Dr. Menninger puts it this way: "When I say a leader must understand men, I don't mean understanding from a common sense point of view alone. I mean from a very uncommon sense point of view. The kind of a leader that I would wish in many, many high places is the man who has some understanding of personalities, their structure and function, how they work, and who knows of the unreasonableness in all of us and the hostilities we all have."

—Growing numbers of the former mentally ill, with the cooperation of management and labor, are being rehabilitated into productive employment.

—Influential advisors to both labor and management finally are putting across the point that perhaps industry is remiss when it looks upon the neurotic employee as a liability who should be either fired or swept under the rug of some remote department. In a book published recently, one psychiatrist views such an employee as a valuable weathervane—much as miners value canaries in coal pits as alarm-ringers of danger.

—Carrying that point a step farther, top industry executives are beginning to recognize that business administration at all levels is defeating itself and the nation at large when it attempts to screen out emotionally tense employees or job seekers. Dr. Frederick W. Dershimer, who was hired as a full-time psychiatrist for E. I. du Pont de Nemours in 1943, said: "The most valuable people are sometimes screwballs. If you do a good enough screening job you may get people who are perfectly normal. But you will have screened out people who discover things like Nylon."

Mental Health—A Definition

Mental health is a medical goal not only in industry but in agriculture and other occupational fields as well. Here is one definition given at an A. M. A. Rural Health Conference by Dr. J. Lester Henderson, a psychiatrist, while he was chairman of the Mental Health Committee of the Washington State Medical Association: "Mental health is that state of mind and feeling that looks on life as basically good. The mentally healthy individual arises in the morning with confidence in his heart, expectation in his attitude and a grin on his face. He is optimistic and friendly, with a capacity for patience and trust. He can take frustration and disappointment without being embittered. He can find new goals if the ones for which he was trying become unobtainable, and in his prayers he can express feelings and ideas beyond what he could express to his parents."

Those trends are bright spots which could offset darkness as medicine and its allies seek to maintain mental health in our growingly complex occupational environment. An over-riding benefit might easily be overlooked in this search. It represents the greatest reward of all: The personal well-being of the nation in generations to come. When a boy hears his father constantly complain about his job, he is likely to have a similar attitude toward his own work and employer. Here we see contagion feeding upon itself. But while there are indications that mental illness may be as communicable as the common cold, there also is ample evidence that mental health in its most beneficial sense is even more "catching." Says Dr. Collins of the A. M. A. Committee:

"The work that men do is an essential part of their lives, not mainly because by it they earn bread but because a man's job gives him stature and binds him to society. The worker who is happy in his job, with confidence in his management and cooperative relations with his coworkers, will spread his contentment throughout the community."

MEDICINE AT WORK in future issues

- *Medical Research Heroes*
- *Hobbies Help Practice*
- *Suicide—A Medical Problem*
- *Hypnosis—Tool or Weapon?*
- *Medical Museums*
- *Health Problems in Education*
- *Safety at Home*

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

Editor and Managing Publisher . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Assistant Editors . . . . . WAYNE G. BRANDSTADT, M.D.
FREDERIC T. JUNG, M.D.
EDWARD R. PINCKNEY, M.D.
Assistant to the Editor . . . . . MILTON GOLIN
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.
News Editor . . . . . CHARLES CHAPMAN

Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

CHILDREN IN HOSPITAL

FOR A CHILD to be removed from his parents, placed in strange surroundings, and subjected to a variety of unpleasant procedures is apt to be psychologically traumatic under the best of circumstances. The extent of such a trauma depends on such factors as the age of the child, the length of his hospitalization, the closeness of the parent-child relationship prior to admission, how well he was prepared for the new experience, the nature of the child's illness, the nature of the required treatment, the basic personality of the child, the frequency of parental visits, the type of nursing care provided, and the presence of other children on the ward. Illingworth [1] elaborates on many of these factors. A child naturally has a feeling of helplessness but this does not cause undue anxiety unless the situation appears to the child to be a threatening one. If an anesthetic must be given the child may fear that he will be or that he has been mutilated while he is or was asleep.[2] Often the child's anxiety is a direct reflection of the anxiety of the parents.

Illingworth calls attention to the fact that the child who cries when parent leaves after admission or at the end of every visiting hour is an overdependent child who also cried when left at home with a sitter for a few hours. Immature parents unconsciously encourage this because they feel flattered by such a show of dependence or, as they prefer to call it, devotion. There is no doubt that parental factors can aggravate the psychological problems of a child in a hospital. These include a poor parent-child relationship before admission, lack of appropriate preparation for admission, failure to visit the child daily, failure to maintain reasonable discipline even in a sick child, and making promises that cannot be kept such as promising that child can come home "tomorrow." The worst type of parent-induced anxiety possible results from the practice of some ignorant parents of telling a well child that if he does not behave the doctor will come and take him to the hospital. Woe betide such a parent if the child ever does have to go to the hospital. The manifestations of psychic trauma in a child who stays in hospital only a short time may be crying, becoming abnormally subdued, poor appetite, enuresis, or tantrums. After a long stay a child may show general apathy and on return home he may react with regression to infantile behavior such as enuresis, excessive clinging, nightmares, fearfulness, tantrums, or speech difficulties. The commonest fears are fear of the dark; of strangers; of nurses, doctors, or anyone dressed in white; and of strange places.

Anything that can be done to prevent or minimize the psychic trauma attendant on the hospitalization of children is almost sure to be worth the effort. Some admissions could be avoided through greater use of a good outpatient service. If a child must be admitted and it is not an emergency, a preliminary visit to the hospital will make the surroundings less unfamiliar especially if the child can meet the nurse who will take care of him and see that other children there are reasonably happy. Some hospitals give parents helpful pamphlets about preparing a child for hospitalization and provide the child with a coloring book emphasizing the pleasant aspects of the projected stay. On admission it is well to allow the mother to stay with the child until he is in bed and has had a few minutes to adjust to his surroundings, or, if the child is not too sick, he should be admitted to the ward playroom instead of bed. Adjustments are always easier in a children's hospital where personnel and facilities are all geared to the needs of the child. If the child must be admitted to a general hospital it should be to a children's ward. Daily visiting by parents should be encouraged. Even though a child cries when his parent leaves it is better that he be upset for a few minutes every day than to feel that he has been deserted or is being punished.

Nurses on duty in a children's ward should pick up and cuddle the smaller children and must learn to recognize that a quiet child is not necessarily a

1. Illingworth, R. S.: Children in Hospital, Lancet **2**: 165-171 (July 26) 1958.
2. Goldman, H. B., and Crain, I.: Psychologic Aspects of Tonsillectomy, New York J. Med. **57**: 232-238 (Jan. 15) 1957.
3. Spence, J.: Doctor, Nurse, and Sick Child, Am. J. Nursing **51**: 14-15 (Jan.) 1951.
4. Deleted on proof.
5. Francis, L., and Cutler, R. P.: Psychological Preparation and Premedication for Pediatric Anesthesia, Anesthesiology **18**: 106-109 (Jan.-Feb.) 1957.

good child or that a child who cries or shouts is not necessarily a bad child. The nurse should act as a mother substitute and do all in her power to comfort a distressed child whatever the cause of the distress may be.[4] Some hospitals allow the mother to be admitted as a companion if the child is under 5 and is in for a short stay. This provides a good experience for the mother in how to care for a sick child, permits the child to retain a feeling of security, and in some cases (although this should not be so) makes the staff more considerate in their treatment of the child. Insofar as possible the child should be kept busy and if toys are provided they should be of a sort to give scope to his imagination. The diet should be balanced and the food attractively served. When unpleasant procedures are necessary they should be done quickly and as painlessly as possible.

Of all the preventive measures, however, a good parent-child relationship is the best. In explaining to a child that he must go to the hospital the parent should never lie to him. It is unwise to go into elaborate details but important to let child talk and ask questions so that any misconception on his part can be corrected in simple terms. This must be done in a straightforward manner and without trying to shame or ridicule him.[5] After an operation the child should again be encouraged to talk about any fears he may have so that erroneous ideas about what was done can be dispelled. If a child is unduly disturbed emotionally before going into hospital psychotherapy should be given before admission if an emergency operation is not required.

Lest the impression be given that only psychic harm can come from hospitalization it should be added that with proper preparation the experience may be a constructive rather than a traumatic one in that it aids the child in growing up and establishing an independent outlook on life. The association with other children and with adults, especially those of a psychologically oriented hospital staff, can also be beneficial.

WOE AND WORK

Only a few years ago wives, sociologists, and clergymen the country over were viewing with alarm the picture of the husband so engrossed in his job that, instead of frolicking with his family at the end of a day's work, he would bring home a briefcase crammed with more business toil. The situation still may be an alarming one, but now there is a kind of reverse phenomenon that poses a more formidable problem: the employee or executive who carries his home troubles to work.

This is a problem of little-realized but huge proportions, affecting not merely the individual and his family but the community and even the nation at large. The economic loss is staggering, the attendant interpersonal impacts are imposing, and the resulting total challenge to medicine is a great one indeed. A special article on page 1363 of this issue in the new Medicine at Work section notes that, while the vast majority of leaders and employees in American business and industry are temperamentally in tune with their jobs, there is enough personal worry and disturbance in their ranks to pose a real threat to the well-being of the labor force.

The threat is a jeopardy to mental health but it also endangers physical health. This is because the worker suffering from "chronic anxiety" stands as a double hazard. On the one hand, personal tensions which may preoccupy his thoughts create a distinct accident peril to himself and fellow employees, particularly where men are clustered around machinery. At the same time, these off-the-job disturbances—whether manifested at work in gripes said aloud or in deep-seated suspicions smoldering silently—carry a germ of communicability which might infect co-workers as surely as a sneeze might infect them with the common cold.

This is where the family doctor can play a starring role. By serving as a case-finder of maladjusted workers in his everyday practice, and following through on a broad scale with early therapy and preventive measures for all of his patients, the physician can achieve a dual purpose: transform a half-happy drudge into an effective and satisfied employee, and help solve a community health problem by raising the level of occupational fitness. The effort may also serve to raise the country's standard of living. For it is a fact that accidents, gold-bricking, excessive work absence, trouble-making, and other signs of employee maladjustment cause a tremendous dollar loss in industrial output. Two industrial psychiatrists in a book published this year estimated the annual loss at "hundreds of millions of dollars." The Chicago business magazine, *Commerce*, figures it closer to three billion dollars a year.

Whatever the cost shown on corporate ledgers, it is the debit in terms of human suffering which is felt the most. Because of the growing urgency of this multiphasic problem, the A. M. A. Board of Trustees last spring directed that a Joint Committee on Mental Health in Industry (under the Councils on Industrial Health and Mental Health) be formed to explore the field. The Committee is scheduled to meet for the first time this month. What it finds, and what it eventually will recommend, should illustrate again that the profession is just as concerned with community building as it is with personal healing.

COUNCIL ON MEDICAL SERVICE

ALABAMA COMMUNITY MEDICAL RATING SURVEY

The Community Rating Schedule, prepared under the direction of the Council's Committee on Medical and Related Facilities, has been utilized in several statewide surveys by medical associations. This schedule was designed to aid a community seeking more medical care to determine (a) the need priority, from the standpoint of the community, and (b) the desirability, from the standpoint of the physician. The state medical associations that have used the schedule have a means of distinguishing the communities that need more medical care from those that either do not need more physicians and/or could not support one.

In 1954, after participation in two regional placement service conferences, sponsored by the A. M. A.'s Council on Medical Service, the Committee on Public Relations of the Medical Association of the State of Alabama established a Physicians Placement Service under the direction of Mr. W. A. Dozier Jr., at that time the association's director of public relations and now the executive secretary of the state medical association. A comprehensive set of questionnaires was developed for the purpose of securing pertinent data from physicians seeking a location for practice and from communities seeking a physician. The physicians were given the information on communities seeking more medical care and the communities were supplied with the names of physicians interested in a location; after that it was up to the community and the physician to make their own contacts and arrangements. After the service had been in operation for four years, the Alabama Committee on Public Relations reviewed this phase of their program, as well as related statistics on the distribution of medical care in the state. It was noted that Alabama, with a 1957 population of 3,061,743 and 2,239 physicians, had a population-physician ratio of 1,367. The population-physician ratio by individual county ranged from 954 to 7,435, with a minimum of two physicians in any county. During each of the past five years there had been a net gain in the number of new physicians in the state over the total number lost by death and by removal to other states. It was found that approximately one-third of the physicians requesting location information had been directly or indirectly placed by the Alabama Physicians Placement Service. In order to better serve the steadily increasing number of physicians requesting location information and communities seeking additional medical care, the Committee felt that this would be an opportune time for a community medical rating survey.

Purpose

To those interested in making the survey, the sixfold purpose of the proposed study fell into the following areas: "(1) To determine where and to what extent additional medical care is needed; (2) To assist physicians in locating in communities where they can practice to the full extent of their training; (3) To evaluate the medical desirability of a given location from the standpoint of a physician seeking a place to practice; (4) To assist communities in improving their medical desirability rating; (5) To submit statistical information to corroborate the facts revealed in this survey; (6) To assist the State Board of Censors in placing to the best advantage the six students, now on state scholarships at the University of Alabama Medical College, who have agreed to practice in communities of 10,000 population or less, when they graduate."

Procedure

The Committee on Public Relations appointed a Survey Committee composed of J. Michaelson, M.D., Foley, chairman of the Committee on Public Relations; R. O. Rutland Jr., M.D., Fayette, chairman of the subcommittee on physician placement; and Mr. W. V. Wallace, Montgomery, executive assistant of the Medical Association of the State of Alabama. The president of the medical society in each county to be surveyed was requested to ask one member of his society to serve as a representative on the Committee when a town in his area was under evaluation.

Initially, the town clerks of 301 Alabama municipalities, with a population of 25,000 or under, were sent a questionnaire relative to the available medical care in the area. An accompanying letter of explanation was co-signed by Mr. W. V. Wallace, member of the Committee, and by Mr. E. E. Reid, executive director of the Alabama League of

Municipalities. In the cases where a response was not received to the first letter, a second letter and form covering county information was sent to the president of the local Chamber of Commerce. Concurrently, E. Julian Hodges, M.D., Scottsboro, president of the Alabama Academy of General Practice, mailed a similar questionnaire and letter of explanation to an Academy member in each county. Follow-up letters were sent where necessary to secure a response. These combined mailings brought replies from one or more towns in 62 of the 67 counties in the state.

After the questionnaires were returned and tabulated, the Survey Committee made a pilot study of three towns: Phil Campbell (population, 758), Coffeeville (211), and Grove Hill (1,443). Three weeks prior to the visit to each community, letters of explanation, including the date for a scheduled visit by the Committee, were sent to the communities and also to the president and secretary of the respective county medical societies, inviting them to attend the community medical evaluation meeting. At each of these three meetings the Community Rating Schedule was applied by the Committee in conjunction with the local group. Distribution was made in each community of the booklet, "YOUR TOWN . . . . Weighed in the Balance—CAN IT SUPPORT A DOCTOR?" This concise, informative booklet, prepared by the Medical Association of the State of Alabama, raises questions to aid the community in looking at itself, as a new citizen would see it, and offers "suggestions for keeping a doctor once he arrives."

After the compilation of the information secured through visits to these three communities, the program was outlined for the other areas to be visited. The Committee felt that the participation and cooperation of the local physicians was exceptionally good. Mass meetings had not been requested in any community, but attendance by local citizens sometimes reached 65. The visiting committee felt that the discussion on the part of the townspeople showed widespread interest in the problem and also careful preparation for the meeting.

Out of the eight months required to complete the survey, four weeks were used to visit the 38 communities located in 24 counties. Because of the thorough preliminary planning, an average of three communities could be visited each day.

The community surveys have been mimeographed and are being made available to physicians upon request either to the state association or to the Council on Medical Service.

Results

Results of the survey may be listed as follows: First, during the survey the Committee found much community information that would be valuable to a physician seeking a location for practice, but not previously listed in the Alabama Physicians Placement Service files. For example, a number of equipped medical facilities had been built by towns hoping to secure a physician; new industries had been built in a number of areas, as well as new churches, schools, and additional recreational facilities. Second, in the short time since the Community Rating Schedule has been applied, 2 of the 38 towns visited have secured a physician. Third, the 1953 Legislature of the State of Alabama created six state scholarships available each year for medical students at the University of Alabama Medical College in Birmingham. Students who are accepted for this program agree to practice in an Alabama town with a population of 10,000 or under. If the physician practices in the approved town for five years, he does not have to repay any part of the loan, otherwise he repays the loan as provided by the Alabama law. The first six physicians participating in this program are completing their internship in 1958. The survey offers excellent resource material for these physicians who plan to practice where there is a medical need. Fourth, according to the report prepared by the Committee, "if nothing else were accomplished except the personal contact made with these communities the Committee feels that the time, money and effort involved were justified in enhancing the relationship and prestige of the medical profession in Alabama with these communities."

From the survey statistics it is interesting to note that only 3 of the 62 counties responding to the mailed questionnaire had noticeable discrepancies between the physicians' opinion about the need for more physicians and the laymen's opinion on the matter. In one county the physicians felt the greater need, in the other two the laymen expressed a greater need. The population-physician ratios in these counties were 1,601, 1,258, and 954. The report that has been prepared does not mark the end of the Alabama Community Rating Program. The Survey Committee is to become a permanent part of the Committee on Public Relations. An evaluation visit will be made to each new community to be listed by the Alabama Physicians Placement Service.

The physicians of Alabama, their association staff, and the laymen of the state are to be commended, first, for their recognition of the fact that more medical care is needed in the state, second, for their cooperative study to determine where the need is greatest, and third, for their plans, already in operation, to do something concrete to bring more medical care to areas in need.

MEDICAL NEWS

CALIFORNIA

Dr. Farber Appointed Assistant Dean.—Dr. Seymour M. Farber, head of the continuing education program at the university medical center since 1955, has been appointed assistant dean of the University of California School of Medicine, San Francisco. Postgraduate medical education will be Dr. Farber's area of special responsibility. About 2,500 practicing physicians participate annually in the postgraduate courses at the medical center in cooperation with bay-area hospitals and in outlying northern California communities. These courses range from the one-day symposium to a full-time three-months' course in the use of radioisotopes. Other assistant deans of the medical school are Drs. Robert H. Crede and Malcolm S. Watts. Dr. Leon Goldman is associate dean.

New Cardiovascular Research Institute.—At the dedication of the Cardiovascular Research Institute October 30 at the University of California Medical Center, San Francisco, the principal speaker was the Honorable Earl Warren, Chief Justice of the United States Supreme Court. Others participating in the dedication were president Clark Kerr of the University of California Medical Center; Dr. John B. D. M. Saunders, dean of the School of Medicine, and Dr. Julius H. Comroe, Jr., director of the Cardiovascular Research Institute. The institute, which occupies the 13th floor of the new Herbert C. Moffitt Hospital, brings together members from 13 departments of the School of Medicine and more than 20 research fellows and trainees. Its laboratories, which have already been occupied for several months, are devoted to basic and clinical studies of the functions and diseases of the circulatory system and related organs. Dr. William J. Kerr, emeritus professor of medicine, proposed the establishment of the institute before World War II. After the war appropriations for building the Moffitt Hospital included funds to construct the shell of an additional floor for the eventual use of such an institute. Among the agencies and organizations that have made grants to complete this floor and purchase laboratory equipment are the U. S. Public Health Service, California Department of Health, and the Heart Associations of Alameda, Merced, San Diego, San Francisco and Yolo Counties.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

CONNECTICUT

State Society's Clinical Congress.—The 33rd clinical congress of the Connecticut State Medical Society and the Yale University School of Medicine, New Haven, was held Nov. 5 in Hartford featuring nine illustrated lectures on new advances in surgery and patient care on subjects such as modern treatment of infectious diseases, care of staphylococcal infections in infants, use of drugs in kidney ailments, degeneration of the arteries, advances in gastrointestinal surgery, methods of nutrition in surgical patients, and treatment of illness in pregnancy. The program was arranged by the society's Committee on Postgraduate Education on which Dr. Arthur Ebbert Jr., assistant dean, Yale University School of Medicine, was chairman.

DISTRICT OF COLUMBIA

Annual Scientific Assembly.—The 27th annual scientific assembly of the Medical Society of the District of Columbia will be held in the Statler Hilton, Washington, D. C., Nov. 24-26. The scientific program will comprise a series of conferences, workshops, and panel discussions on congestive heart failure, fluid and electrolytes, recent advances in virology, problems in the management of surgical patients, toxemia of pregnancy, every-day psychiatry in general office practice, discussions on general questions, and clinicopathologic conference. There will also be a medical motion picture program, exhibits, luncheon meetings sponsored by the George Washington University Medical Society and the Georgetown University Medical Alumni Association. A benefit buffet supper for the Woman's Auxiliary's Nursing Fund and the annual dinner for doctors office staffs are planned. Active and life members are entitled to one ticket without charge to the Medical Society's luncheon on Monday. Nonmembers and associate and affiliate members may purchase luncheon tickets for $3.75 each.

GEORGIA

Conference on Nutrition in Athens.—"Better Foods for Better Nutrition," will be the theme of a joint Conference sponsored by the Divisions of Foods and Nutrition, and Food Procession of the University of Georgia to be held March 4-6, 1959, at The Center for Continuing Education, University of Georgia, Athens. This Conference is planned for persons engaged in research, extension, and teach-

ing of foods and nutrition. Special attention will be given to industrial and institutional problems in processing, handling, and serving foods.

ILLINOIS

Chicago

Lecture on Growth and Genetics.—The Chicago Medical School and the Squibb Centennial Lecture Committee will present Theodore T. Puck, Ph.D., chairman, department of biophysics, University of Colorado Medical Center, Denver, in a lecture, Nov. 10, in the Sarah Morris Amphitheatre, Michael Reese Children's Hospital, at 4:00 p. m. The subject will be "Growth and Genetics of Somatic Mammalian Cells in Vitro." Again, on Nov. 12, at 9:30 a. m., at Mount Sinai Hospital, Dr. Puck will address a seminar on the application of single cell plating techniques to problems in medicine. Both meetings are open to those interested.

Heart-in-Industry Conference.—The 6th Heart-in-Industry conference, sponsored by the Chicago Heart Association and the Chicago Association of Commerce and Industry, will be Friday, November 14, at the Hotel Sherman. This conference was made possible by a grant from the Visking Corporation of Chicago as a memorial to the late Gustav Freund II. In several workshop groups, the discussions will concern a review of two case histories of workers with cardiac disease. The featured speaker at the luncheon will be Dr. Paul Dudley White of Boston. Following adjournment at 2:00 p. m., all participants are invited to attend a special discussion by the Illinois Governor's committee on employment of the physically handicapped in the Bal Tabarin Room of the Sherman Hotel.

KENTUCKY

State Medical Election.—At the annual meeting of the Kentucky State Medical Association, Louisville, Sept. 23-25, the following officers were elected: Drs. Robert W. Robertson, Paducah, president; Irvin Abell Jr., Louisville, president-elect; Marvin A. Lucas, Louisville, Thomas O. Meredith Jr., Harrodsburg, and Lillard F. Beasley, Franklin, vice-presidents; Woodford B. Troutman, Louisville, secretary (re-elected); and Delmas M. Clardy, Hopkinsville, treasurer.

MARYLAND

Dr. Wilbur Will Give Friedenwald Lecture.—The 11th annual Friedenwald Memorial Lecture on the diagnosis and management of functional gastrointestinal disorders will be given November 11 at 5.00 p. m. at the University of Maryland School of Medicine, Baltimore, by Dr. Dwight L. Wilbur, clinical professor of medicine at Stanford University School of Medicine, San Francisco, and president of the American College of Physicians.

MASSACHUSETTS

Benjamin Waterhouse Society.—The Benjamin Waterhouse Medical History Society will meet at the Massachusetts Memorial Hospital, Nov. 17, when, following a dinner for members and guests, Dr. Carl W. Walter, associate clinical professor of surgery, Harvard Medical School, Boston, and surgeon, Peter Bent Brigham Hospital, will lecture on "Asepsis in the 19th Century." All persons interested are invited to attend the medical history session. The president of the society is Dr. Lamar Soutter and the secretary is Dr. John J. Bryne, both of Boston.

Dr. Hastings Goes to California.—A. Baird Hastings, Ph.D., head of the biological chemistry department at Harvard, will retire December 31 then join the Scripps Clinic and Research Foundation at LaJolla, California, where he will continue his research in intermediary metabolism and in the application of biochemistry to the study of disease. At Harvard he will become Hamilton Kuhn of biological chemistry emeritus, the second to hold that professorship; the first of whom was Dr. Otto K. O. Folin. Dr. Hastings was appointed professor of physiological chemistry at the University of Chicago in 1926. He joined the faculty at Harvard in 1935 as head of the biological chemistry department.

The William James Lectures.—Harvard University has announced that Donald B. Lindsley, Ph.D., professor of psychology and physiology, University of California School of Medicine, Los Angeles, will give nine William James Lectures on successive Mondays beginning October 20; thus the next lecture in this series will be November 10 in the Allston Burr Lecture Hall A, 4:15 p. m. The general subject of the series is "Brain Organization and Behavior." The announcement states that the lectures will deal with new knowledge of the nervous system that has certain importance. Prof. Lindsley is said to be best known for his work with the electroencephalograph. Formerly he was a fellow of the National Research Council in the Harvard University physiology department, assistant professor at Brown University, and professor of psychology at Northwestern University.

MICHIGAN

University Gifts and Grants.—Gifts and grants accepted by Wayne State University's Board of Governors, Aug. 20, included $120,670 from the U. S. Public Health Service, to be used in various research projects. From the Michigan Heart Association, $53,050.50 will be used to continue research on heart disease. A total of $45,500 was accepted from the McGregor Fund, of which the department

of psychiatry will get $24,000, while $21,500 will support a program in psychotherapy over a two year period under the direction of Ross Stagner, Ph.D., College of Liberal Arts. The Kresge Foundation presented $31,000 to continue research in neurological sciences under the direction of Dr. Elisha S. Gurdjian of the College of Medicine. The Receiving Hospital Corporation gave $25,000 to be added to the fund to defray salaries of individuals employed in departmental research activities at the College of Medicine.

MINNESOTA

Surgical Travel Fund.—The Regents of the University of Minnesota accepted in July, 1952, from the late Dr. Walter M. Boothby of the Mayo Clinic and Dr. William R. Lovelace, II, of the Lovelace Foundation, Albuquerque, New Mexico, a gift of $18,000, representing accumulated royalties from the manufacture of the Boothby-Lovelace oxygen mask. This fund was set up by Drs. Boothby and Lovelace as a surgical travel fellowship under the direction of the Department of Surgery at the University of Minnesota. The earned interest of the fund is being used to permit some of the Trainees of the Department of Surgery to visit other clinics and medical schools.

NEW JERSEY

Slide Seminar on Unusual Tumors.—The eighth annual slide seminar on unusual tumors, sponsored by the New Jersey Society of Pathologists and the New Jersey State Health Department, will be held December 6 at the Essex House, Newark, New Jersey at 2:00 p. m. Case histories and micro slides are being mailed to all members of the society. Dr. Arthur P. Stout of Columbia University College of Physicians and Surgeons, New York, will act as moderator. Dr. Jacob Churg of Teaneck, chairman of the program committee, and Elmer L. Shaffer, Ph.D., will represent the New Jersey State Department of Health. All interested physicians are invited to attend.

NEW YORK

Army Reserve Hospital Moves to New Headquarters.—The 307th General Hospital, a 1,000 bed U. S. Army Reserve Unit, outgrew the space and facilities at its training center on West 44th Street, New York City, and has moved to new headquarters on the St. John's University campus at Hillside, Jamaica. This unit, which is now at full strength, underwent its annual summer training period in August at Ft. Dix, New Jersey. Most of the commissioned and non-commissioned officers have had active service in either World War II or Korea and nearly all members of the hospital detachment are either high school or college graduates. Col. Gerald D. Dorman, M. C., New York City, a member of the House of Delegates of the American Medical Association, has been in command of the 307th General Hospital ever since it was activated in July, 1955.

Wadsworth Lecture.—The ninth Augustus B. Wadsworth Lecture is to be given at the Division of Laboratories and Research, New York State Department of Health, Albany, Nov. 20. Dr. Albert H. Coons, investigator for the American Heart Association and visiting professor of bacteriology and immunology, Harvard Medical School, Boston, will speak on "Stalking with Antibodies." The lectureship was established in 1950 by the staff of the Laboratories and the Council of the New York State Association of Public Health Laboratories.

New York City

Aaron Brown Lecture.—The third annual Aaron Brown lecture, sponsored by the Phi Delta Epsilon Fraternity, Beta XI Chapter, will be delivered February 14, 1959 at 11:00 a. m. at Georgetown University School of Medicine, Washington, D. C. Dr. Bernard J. Alpers, Philadelphia, will speak on "Compensating Mechanisms in Cerebral Blood Flow."

Personal.—Dr. Ammon Walter Hoover has been appointed regional medical officer of the Pennsylvania Railroad's New York region succeeding Dr. John D. Talbert, resigned.——Benjamin W. Zweifach, Ph.D., an investigator of the American Heart Association giving full time to research at New York University College of Medicine, has been promoted to full professor in the department of pathology.

Health Forums for the Public in Brooklyn.—The Brooklyn office of the New York City health department, the Brooklyn Academy of Arts and Sciences and the New York Journal American have joined the Kings County Medical Society in sponsoring a series of health talks to be given at the Brooklyn Academy of Music as follows:

Nov. 19, 1958—Diabetes
Dec. 3, 1958—Tuberculosis
Mar. 4, 1959—Dental Health
Apr. 1, 1959—Cancer
May 6, 1959—Nutrition

Lectures for the Laity.—The 24th series of Lectures for the Laity, presented by the New York Academy of Medicine, 2 East 103 St., began Nov. 5 with the Linsly R. Williams Memorial Lecture, "Fact, Fancy and Corruption in the Interpretation of Science to the Public," by Wallace F. Janssen of the U. S. Food and Drug Administration. The next lecture in this series will be Nov. 19, 8:30 p. m., by Paul F. Lazarsfeld, Ph.D., Columbia University College of Physicians and Surgeons, on "Paths and Roadblocks Between the Natural and the Social Sciences," and

on Dec. 3, 8:30 p. m., Elmer Hutchisson, Ph.D., director of the American Institute of Physics, will discuss "Liberal Education in an Age of Science."

Medical Mobilization for Disaster.—A symposium on medical mobilization for disaster was held at the Kings County Hospital Center in Brooklyn Oct. 25, sponsored by the surgery department of the State University of New York Downstate Medical Center and the trauma service of the Kings County Hospital Center, and in cooperation with the New York State Department of Civil Defense. The speakers were Col. Joseph R. Shaeffer, of the Walter Reed Army Institute of Research, Washington, D. C., Dr. Roald N. Grant, professor of surgery, New York University College of Medicine, Dr. Robert H. Kennedy, director of surgery at the Beekman Downtown Hospital, and Dr. James M. Hershey, of the New York State Department of Health.

NORTH CAROLINA

New Biology Building at Duke.—The site for a new biology-forestry building at Duke University just south of the Physics Building has been cleared and construction is expected to begin this fall. The U. S. Public Health Service has approved a $234,500 grant toward the cost of this building, which is expected to cost a total of 3½ million dollars, and provide facilities for research work in physiology, cytology, serology, biochemistry, biophysics and nuclear chemistry. The zoology department, the botany department and the school of forestry each will occupy a separate wing of the building.

PENNSYLVANIA

Philadelphia

Foundation Grants in New Fields.—Four University of Pennsylvania medical scientists have been awarded grants totaling $245,382 by the March of Dimes of the National Foundation (formerly the National Foundation for Infantile Paralysis). The four scientists are Dr. Arthur B. DuBois, associate professor of physiology and pharmacology; Dr. William Dunbar, coordinator of the rehabilitation program at the University; William F. McLimans, Ph.D., associate professor of research medicine; Dr. Hilary Koprowski, director of the Wistar Institute. The first medical research grants to come to the Philadelphia area from the Foundation under its new policy of supporting work in fields other than poliomyelitis will be in the fields of virus research, tissue culture cell changes, scoliosis, and rehabilitation.

TEXAS

Medical Problems of Space Flight.—A symposium on the foregoing subject at Randolph Air Force Base, Texas, Oct. 28, was sponsored by the School of Aviation Medicine and the Bexar County Medical Society. Col. Paul A. Campbell, chief of the school's Space Medicine Division, surveyed recent research on factors affecting human performance and survival in space. Capt. Jerrold L. Wheaton's paper dealt with the effects of "Isolation and Sensory Deprivation" on flyers under conditions they will meet on flights beyond the earth's atmosphere. Lt. Col. George R. Steinkamp, chief, department of astroecology, discussed studies made by the school in "Closed Ecological Systems."

After dinner, the program continued with a paper on "The Zero Gravity State," by Capt. Willard R. Hawkins of the Space Medicine Division. Dr. Hubertus Strughold, advisor for research concluded the program with a look at the future of human flight in space. The program was arranged by Col. Hamilton B. Webb, chief, Aviation Medicine Division, and Dr. Billy B. Markette, of San Antonio, representing the county medical society. Presiding were Maj. Gen. Otis O. Benson Jr., commandant of the School of Aviation Medicine, and Dr. Charles W. Tennison, president of the Bexar County Medical Society.

UTAH

State Medical Election.—At the annual meeting of the Utah State Medical Association, Sept. 9-12, the following officers were elected: president, Dr. Ulrich R. Bryner, Salt Lake City; president-elect, Dr. I. Bruce McQuarrie, Ogden; honorary president, Dr. Arthur J. Murphy, Salt Lake City; secretary, Dr. J. Poulson Hunter, Salt Lake City; treasurer '60, Dr. Robert M. Dalrymple, Salt Lake City; executive secretary, Mr. Harold Bowman, Salt Lake City.

GENERAL

New Address of Science Foundation.—The National Science Foundation, an independent agency of the United States Government, announces that all offices are now centralized in one building at 1951 Constitution Avenue, Washington 25, D. C., Telephone, Sterling 3-2140.

Society News.—The American Board of Anesthesiology, at its annual meeting October 3, elected the following officers: president, Dr. Curtiss B. Hickcox, Hartford, Conn.; vice president, Dr. Frederick P. Haugen, Portland, Ore.; secretary-treasurer, Dr. Forrest E. Leffingwell, Pasadena, Calif.

Medical Clinics Election.—At the recent annual meeting of the American Association of Medical Clinics in San Francisco, Dr. Joseph W. St. Geme, of Los Angeles, was elected president; Dr. Russell V. Lee, Palo Alto, Calif., vice-president; and Dr. Joseph B. Davis, of Marion, Ind., secretary-treasurer. The next meeting of the association will be at the Blackstone Hotel, Chicago, Sept. 24-26, 1959.

F.B.I. Wants Help in Locating Cole and Conley.—The Federal Bureau of Investigation is trying to locate the following two persons who may apply for treatment at some physician's office:

Fig. 1.—George Edward Cole.

George Edward Cole, alias George E. Cole, George Edward Puckett, George Edward Cole Puckett. Cole is alleged to have shot and killed a San Francisco police officer Dec. 30, 1956, during an attempted holdup of a tavern. Cole fled from California and a federal warrant for his arrest has been issued. This fugitive is armed and is considered extremely dangerous. Cole was born March 24, 1927, in Philadelphia. His height is 6 ft. 1 in.; weight 160 to 178 lb.; build, medium, hair, brown, receding; eyes, brown; complexion, medium; race, white; nationality, American; occupations, bus driver, truck driver, typist. He has a pit scar on outside corner of right eye, small cut scar on inside of left wrist, appendectomy scar, tattoo small heart and names "Mom" and "Dad" and letters "GP" or "SP" on left forearm; tattoo eight-point star on back of left hand; wears full upper denture.

Fig. 2.—Yvonne Conley.

When Cole fled San Francisco it is believed he was accompanied by Yvonne Conley and it is possible this woman is still with him. Yvonne Conley has used the following aliases: Yvonne B. Blunt, Yvonne Broome, Lee Burke, Starr Burk, Yvonne Galipeau, Yvonne Hales, Mrs. V. Q. Hales, Yvonne Mason, Jean Noble, June Noble, and Lee Walker.

Conley has used drugs which in some states require a doctor's prescription. She has been treated for cirrhosis of the liver. She has used Empirin Compound, liver extract, vitamin B_{12}, Premarin, and Amesiec. She was born July 19, 1913, at St. Pierre, Manitoba, Canada. Her height is 4 ft. 11½ in.; weight, 140 lb.; build, heavy; hair, brown; eyes, brown; complexion, dark; race, white. She has a ½ in. cut scar on forehead between eyebrows, ½ in. cut scar under chin, scar on back of left hand, hysterectomy scar, numerous needle marks on hips; some upper teeth reportedly are missing. F.B.I. Number 1,055,332. The San Francisco Police Department, California, holds a warrant charging Conley as Yvonne Galipeau as an accessory to murder.

Any person having information that might assist in locating one or both of these persons is requested to immediately notify the Director of the FBI, Department of Justice, Washington 25, D.C., or the special agent in charge of the nearest FBI Division, the telephone number of which appears on the first page of local telephone directories.

Since Cole is considered extremely dangerous, no person should take any action which would place his or her life in jeopardy.

Grants to Aid Mental Health Workers.—The National Institute of Health, Washington, D. C., has granted $90,000 to the Southern Regional Education Board, 881 Peachtree Street, N. E., Atlanta 9, Georgia, for grants for in-service training of workers in mental institutions in southern states. These grants are available to anyone working on the staff of the mental hospital or training school, including administrative, professional and operational personnel. Persons interested may write to the above address in Atlanta.

Inter-Society Cytology Council.—When this group meets at the Hotel Statler, New York City, Nov. 13-15, the program will include panel discussions on cytology of disseminated cancer, in-situ bronchogenic carcinoma, and round-table discussions on cytology and pathology of early endometrial cancer, sessions on hormonal cytology, gynecologic cytology, cytology of irradiation, a symposium on the cell, medical motion pictures, and scientific and technical exhibits. Members and guests are invited to the annual banquet Thursday evening. Dress is optional. The president of the society is Dr. Emerson Day, New York City, and the president-elect is Dr. John R. McDonald, Rochester, Minn. Information may be obtained from the secretary, Dr. Paul F. Fletcher, 634 N. Grant Blvd., St. Louis 3.

Meeting of Gastroenterology Research Group.—The general subject for the meeting of the Gastroenterology Research Group in Chicago, October 31, was "Absorption of Water and Electrolytes from the

Gastrointestinal Tract." The panel moderated by Dr. Chas. A. M. Hogben, Washington, D. C. and the members of the panel, Eugene D. Grim, Ph.D., of the University of Minnesota; Dr. Isidore S. Edelman of the University of California Medical Center, San Francisco; Jack M. Ginsburg, Ph.D., of the University of Cincinnati College of Medicine; Drs. John F. Scholer of Palo Alto, California; Chas. F. Code, Mayo Clinic, Rochester; John T. Farrar of Cornell University Medical College, New York, and Donald W. Seldin of the University of Texas Southwestern Medical School, Dallas.

Interstate Postgraduate Medical Association.—The 43rd international meeting of the Interstate Postgraduate Medical Association will be at the Statler-Hilton Hotel, Cleveland, Ohio, November 10-13, under the presidency of Dr. Tom D. Spies, Birmingham, Alabama. In addition to a scientific program featuring distinguished speakers on various subjects, Mr. Charles F. Kettering, scientist, will address the annual dinner Wednesday evening on "An Inventor Looks at Science and Medicine." There will be exhibits, teaching films and a program of entertainment for the ladies. The registration fee is $10.00 except for physicians in the armed forces, residents and internes, graduate nurses, technicians and dieticians ($2.00). A complete program of this meeting may be obtained by writing to the Interstate Postgraduate Medical Association, Box 1109, Madison 1, Wis.

Cancer Seminar in Tampa, Florida.—The ninth biennial meeting of the Southeastern States Cancer Seminar will be at the Hillsboro Hotel, Tampa, Fla., Nov. 19-21, presented by the Hillsborough County Medical Association and sponsored by the Florida Division of the American Cancer Society and the Florida State Board of Health, in cooperation with the Florida Medical Association. In addition to panel discussions on various aspects of cancer, there will be individual presentations including among others the following guest speakers: Drs. Joseph P. Concannon, Jefferson Medical College of Philadelphia; August R. Crane, University of Pennsylvania School of Medicine, Philadelphia; Ruben Flocks, State University of Iowa College of Medicine, Iowa City; Simon Kramer, Jefferson Medical College of Philadelphia; Stanley L. Lane, Albert Einstein College College of Medicine of Yeshiva University, New York; Joseph V. Meigs, Harvard Medical School, Boston; James L. Pipkin, Baylor University Post-graduate School of Medicine, Houston, Texas; James D. Rives, Louisiana State University School of Medicine; Herbert E. Schmitz, Stritch School of Medicine of Loyola University, Chicago; Max M. Strumia, University of Pennsylvania Graduate School of Medicine, Philadelphia; and Kenneth W. Warren, of the Lahey Clinic, Boston.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Oct. 11, 1958 Paralytic Type	Oct. 11, 1958 Total Cases	Oct. 12 1957 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	2	2	1
Rhode Island	..	..	..
Connecticut	3	3	3
Middle Atlantic States			
New York	11	16	12
New Jersey	7	17	1
Pennsylvania	3	7	..
East North Central States			
Ohio	8	19	6
Indiana	5	9	3
Illinois	3	10	22
Michigan	36	98	23
Wisconsin	2	3	2
West North Central States			
Minnesota	3	4	1
Iowa	..	..	1
Missouri	14	15	2
North Dakota	..	3	..
South Dakota	..	..	..
Nebraska	..	3	1
Kansas	..	3	..
South Atlantic States			
Delaware	1	1	1
Maryland	1	1	2
District of Columbia	..	..	1
Virginia	10	12	5
West Virginia	5	17	1
North Carolina	..	..	8
South Carolina	..	1	5
Georgia	..	..	1
Florida	7	12	3
East South Central States			
Kentucky	2	4	4
Tennessee	6	8	4
Alabama	..	1	4
Mississippi	2	3	1
West South Central States			
Arkansas	..	..	..
Louisiana	..	..	5
Oklahoma	..	..	2
Texas	10	16	14
Mountain States			
Montana	1	1	2
Idaho	..	..	..
Wyoming	..	1	..
Colorado	..	1	1
New Mexico	1	4	2
Arizona	1	2	3
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	5	1
Oregon	..	..	..
California	8	9	19
Territories and Possessions			
Alaska	..	..	..
Hawaii	2	2	1
Puerto Rico	..	..	1
Total	134	313	169

American College of Cardiology.—The seventh interim meeting of the American College of Cardiology will be at the Jung Hotel, New Orleans, La., Nov. 20-22. The presentations before the scientific session Thursday afternoon will be by the New Orleans group. Fireside conferences comprising five individual presentations will be held Thursday evening, 8:30 to 10 p. m. A symposium on "Diagnosis of Arterial Disease" will comprise the second scientific session Friday morning, and a symposium on "Medical Treatment of Arterial Disease" will be held Friday afternoon. On Saturday morning will be the symposium on "Surgical Treatment of

Peripheral Arterial Disease," and six scientific papers will be presented by members on Saturday afternoon. The program for the ladies includes a luncheon Thursday and then a tour of the famous French Quarter. After breakfast at Brennan's Friday morning, buses with guides will take the ladies on a tour of the city. There will be a banquet Friday evening (dress optional).

FOREIGN

Smallpox in Pakistan.—The government of Pakistan recently requested help from the World Health Organization in dealing with the worst smallpox epidemic Pakistan has experienced since that country was created in 1947. In complying, WHO shipped two million doses of smallpox vaccine to Pakistan. According to the September Chronical of the WHO, preliminary estimates indicate that in the first five months of 1958 there were more than 35,500 smallpox cases, with 15,800 deaths in Pakistan. In 1957 the number of cases of smallpox in this country was said to be almost 25,000.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application is Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application is Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *Part I.* Various parts of the United States and Canada, January 16. Candidates notified of their eligibility to participate in Part I must submit their case abstracts within thirty days of notification of eligibility. No candidate may take the written examination unless the case abstracts have been received in the office of the Secretary. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), Various Cities, Jan. 26. *Oral.* Philadelphia, June 3-6. Sec., Dr. Merrill J. King, 22 White St., Rockland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pediatrics: *Oral.* New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Boston, May 9-11. Final date for submitting case reports is Jan. 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Regular Examination.* Washington, D. C., Dec. 8-11. Final date for filing application was July 1. *Special examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology.* Washington, D. C., Dec. 6. Final date for filing application was Oct. 1. *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application is Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications was August 1. *Part II.* New York City, Dec. 15-16; Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Oral.* Los Angeles, April. Final date for filing application is Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

DEATHS

Bliss, Rodney Waldo, Oklahoma City, Okla.; Rush Medical College, Chicago, 1904; professor of medicine emeritus and chairman of the department at the University of Nebraska College of Medicine, Omaha; member of the Nebraska State Medical Association; an associate member of the American Medical Association; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served on the staffs of the Nebraska Methodist and University of Nebraska hospitals; died Sept. 5, aged 80.

Boyden, Guy Lee Ⓜ Portland, Ore.; born in Brookings County, S. D., Feb. 17, 1885; Northwestern University Medical School, Chicago, 1911; on July 1, 1911 entered the Mayo Clinic, Rochester, Minn., where he served an internship and residency at St. Mary's Hospital; from 1913 to 1921 practiced medicine in Pendleton, Ore.; veteran of World War I; clinical professor and head, department of otology, rhinology and laryngology, University of Oregon Medical School; was the guest of honor at a meeting in 1958 in San Francisco of the Section on Laryngology, Otology and Rhinology of the American Medical Association, of which he was vice chairman in 1954-1955; past-president of the Oregon Academy of Ophthalmology and Otolaryngology and the Pacific Coast Ophthalmology and Otolaryngology Society; member of the American Laryngological, Rhinological and Otological Society, of which he was at one time vice-president and western chairman; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; associated with the Multnomah Hospital, Emanuel Hospital and St. Vincent's Hospital and Doernbecker Memorial Hospital for Children; in 1955 received an honorary doctor of science degree from South Dakota State College of Agriculture and Mechanic Arts, Brookings; died Sept. 9, aged 73.

Brown, Charles W., Ⓜ St. Louis; St. Louis College of Physicians and Surgeons, 1890; formerly practiced in Caruthersville, Mo.; died Sept. 4, aged 93.

Buck, Samuel Bernice, Anderson, Mo.; University of Maryland School of Medicine, Baltimore, 1904; died in the Veterans Administration Hospital, Fayetteville, Ark., Aug. 28, aged 78.

Carnathan, William George Ⓜ Dallas, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1921; specialist certified by the American Board of Psychiatry and Neurology; service member of the American Medical Association; member of the American Psychiatric Association; at one time on the faculty of his alma mater and Baylor University College of Medicine; from 1942 to 1946 associated with the Texas State Guard; on the staff of the Veterans Administration; died in the Dallas Medical and Surgical Clinic July 8, aged 67, of myocardial infarction.

Cates, Albert, Oklahoma City, Okla.; Memphis (Tenn.) Hospital Medical College, 1906; an associate member of the American Medical Association; served as county health superintendent of public health; died Sept. 4, aged 78, of hypertension and cerebrovascular disease.

Colleran, John Patrick, South Deerfield, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1928; member of the Massachusetts Medical Society; school physician in South Deerfield; on the staffs of the Farren Memorial Hospital in Montague City, and Franklin County Public Hospital in Greenfield; died Sept. 8, aged 55, of cancer of the pancreas.

Cook, Byron Llewellyn Ⓜ Minden, La.; Louisiana State University School of Medicine, New Orleans, 1938; member of the American Academy of General Practice; past-president of the Fourth District Medical Society; veteran of World War II; died in the Schumpert Sanitarium, Shreveport, Aug. 31, aged 44, of disseminated lupus erythematosus.

Cosgrove, Edgar Francis Ⓜ Pittsburgh; University of Pittsburgh School of Medicine, 1936; assistant professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War II; past-president of the Western Pennsylvania Heart Association; associated with Woman's Hospital and the Presbyterian Hospital, where he died Sept. 3, aged 49.

Cowles, Robert Sebastian Ⓜ Greeneville, Tenn.; University of Nashville Medical Department, 1910; past-president of the Greene County Medical Society; for many years county health officer; died Aug. 27, aged 66.

Criss, Ralph J., Coffeeville, Miss; University of Nashville (Tenn.) Medical Department, 1904; died Sept. 11, aged 82.

Davis, James Ethelbert Ⓜ Dexter, Mich.; born in Woodstock, Ont., Oct. 3, 1870; Detroit College of Medicine, 1896; also a graduate in pharmacy; for many years professor of pathology at his alma mater, now known as the Wayne University College of Medicine; served as director of the department of pathology at the University of Detroit Dental

Ⓜ Indicates Member of the American Medical Association.

Department, and extramural lecturer in pathology at the University of Michigan Graduate Medical School; originated the Beaumont Lectureship Foundation; past-president and for many years trustee of the Wayne County Medical Society; past-president of the Alumni Association of the Detroit College of Medicine and Surgery; for many years secretary of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; served on the staffs of the Providence, St. Mary's, and Receiving hospitals; died in the Woodstock (Ont.) General Hospital Aug. 16, aged 87, of coronary thrombosis.

Deak, Alexander Paul ⊗ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1924; died in the Presbyterian Hospital Sept. 2, aged 60.

Decatur, Edwin Forrest ⊗ Kingston, N. H.; Tufts College Medical School, Boston, 1939; member of the American Society of Anesthesiologists; chief of the anesthesiology department at Exeter (N. H.) Hospital, where he was past-president of the medical staff, and where he died Aug. 29, aged 45.

De Pree, John Nelson Warren ⊗ Palouse, Wash.; Rush Medical College, Chicago, 1939; member of the American Academy of General Practice; on the staff of the Gritman Memorial Hospital in Moscow; served as president of Whitman County Medical Society; died in Spokane Sept. 4, aged 49.

Dias, Joseph Lawrence, Tampa, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1903; an associate member of the American Medical Association; at one time practiced in Newark, N. J., where he was on the staff of Hospital of St. Barnabas; member of the Medical Society of New Jersey; formerly on the staff of the Veterans Administration Hospital in Lake City; died in St. Joseph's Hospital Sept. 3, aged 77, of cerebrovascular thrombosis and cancer of the pancreas.

Dixon, Robert Emmett ⊗ Alberta, Ala.; University of Alabama School of Medicine, Mobile, 1917; died Aug. 22, aged 66, of leukemia.

Downes, John Raymond ⊗ Newark, Del.; University of Maryland School of Medicine, Baltimore, 1904; formerly health officer of Queen Anne County; served as city councilman; deputy state health officer for rural New Castle County from 1931 to 1949 when he retired; veteran of World War I; died in the Veterans Administration Hospital, Wilmington, Sept. 4, aged 79.

Doyle, Francis Joseph, Fort Lauderdale, Fla.; Long Island College Hospital, Brooklyn, 1902; died July 18, aged 80, of congestive arteriosclerotic heart disease.

Durburg, John Russell ⊗ Chicago; Loyola University School of Medicine, Chicago, 1934; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served on the faculty of his alma mater; veteran of World War II; member of the staff of St. Joseph's Hospital; died in Cape May, N. J., Sept. 15, aged 48.

Everist, Guy Vernon ⊗ San Diego, Calif.; St. Louis University School of Medicine, 1935; veteran of World War II; served on the staffs of various Veterans Administration hospitals; found dead in his car Sept. 3, aged 50.

Foot, Nathan Chandler, New York City; born in New York City July 27, 1881; Columbia University College of Physicians and Surgeons, New York City, 1907; emeritus professor of surgical pathology at Cornell University Medical College, where he was professor of surgical pathology from 1932 to 1948, and where he did research in cancer detection in the department of pathology; from 1912 to 1919 assistant instructor and instructor of pathology at Harvard Medical School, Boston, where he became instructor of comparative pathology, serving until 1922; assistant professor, associate professor, and professor of pathology at University of Cincinnati College of Medicine from 1922 to 1932; served as research consultant in pathology at the Armed Forces Institute in Washington, D. C.; an associate member of the American Medical Association; fellow of the College of American Pathologists; member and past-president of the American Association of Pathologists and Bacteriologists; member of the American Society of Experimental Pathology, New York Academy of Medicine, New York Pathological Society, of which he was past-president, Harvey Society, American Association for the Advancement of Science, Phi Rho Sigma, Sigma Xi, and Alpha Omega Alpha; corresponding member of the Pathological Society of Argentina; member of the Intersociety Cytology Council; past-president of the American Board of Pathology; served as president of the New York Physicians Art Club; surgical pathologist at the New York Hospital from 1932 to 1948 when he became consultant; author of two textbooks, "Pathology in Surgery" and "Identification of Tumors"; died in the New Rochelle (N. Y.) Hospital Sept. 4, aged 77.

Freeman, Rowland Godfrey Jr., ⊗ Boston; Columbia University College of Physicians and Surgeons, New York City, 1921; member of the American Psychiatric Association and the Association for Research in Nervous and Mental Disease; formerly on the faculty of Tufts College Medical School; in 1937 appointed assistant psychiatrist of the Judge Baker Guidance Center in Boston; veteran of World War II; formerly clinical director at Blytheville in Greenwich, Conn.; died in the Peter Bent Brigham Hospital, Boston, July 23, aged 62, of pulmonary embolism.

Gilbert, Edwin Carpenter, Longmeadow, Mass.; Yale University School of Medicine, New Haven, Conn., 1906; veteran of World War I; for many years trustee of the Belchertown (Mass.) State School; formerly practiced in Springfield, where he served on the staff of the Springfield Hospital, and past-president of the Chamber of Commerce and Rotary Club; died in the Brattleboro Retreat, Brattleboro, Vt., Aug. 23, aged 76, of bronchopneumonia and cerebral arteriosclerosis.

Gilmer, Roy Jones, New Haven, Conn.; Meharry Medical College, Nashville, Tenn., 1942; veteran of World War II; physician for the local welfare department; on the staffs of the Grace-New Haven Community Hospital and the Hospital of Raphael, where he died Aug. 30, aged 42, of coronary thrombosis.

Girvin, Richard Bates ⊗ Minneapolis; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1908; member of the Aero Medical Association; veteran of World War I; in 1940 appointed medical examiner for the Civil Aeronautics Authority; on the staffs of St. Barnabas and St. Andrews hospitals; died in the Barnes Hospital, St. Louis, Aug. 7, aged 74, of emphysema.

Gregg, Ulysses Sherman, Kalamazoo, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1909; served on the staff of the Kalamazoo State Hospital; honorary member of the medical staff, Bronson Methodist Hospital, where he died Aug. 27, aged 78, of cerebral thrombosis.

Hardie, Julian Carter, Salt Lake City; University of Pennsylvania School of Medicine, Philadelphia, 1911; retired in 1947 as county physician; physician and surgeon for the Utah Copper Company and U. S. Fuel Company in Garfield and Hiawatha, Utah; died Aug. 17, aged 83, of bronchopneumonia.

Haynsworth, Custis Hall ⊗ Greenville, S. C.; Medical College of South Carolina, Charleston, 1941; interned at the Central Dispensary and Emergency Hospital in Washington, D. C.; served a residency at the Shriners Hospital for Crippled Children in Greenville, Roper Hospital in Charleston, and the Hospital for Special Surgery in New York City; chief of orthopedic service at the Greenville General Hospital; died Aug. 15, aged 43.

Helland, John William ⊗ Spring Grove, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; died in La Crosse (Wis.) Lutheran Hospital Aug. 28, aged 80.

Hochwald, Adolf, Ray Brook, N. Y.; born in Tesin, Czechoslovakia, Sept. 5, 1906; Masarykova Universita Fakulta Lekarska, Brno, Czechoslovakia, 1930; specialist certified by the American Board of Pathology; member of the American Association of Pathologists and Bacteriologists, Medical Society of the State of New York, American Association for the Advancement of Science, and the Cleveland Society of Pathologists; fellow of the College of American Pathologists; instructor in pathology at the Woman's Medical College of Pennsylvania in Philadelphia, 1943-1944; senior instructor in pathology at Western Reserve University School of Medicine in Cleveland, from 1948 to 1951; served as assistant professor of pathology at the New York University College of Medicine; formerly on the staffs of the Mount Sinai Hospital in Cleveland and University Hospital (New York University–Bellevue Medical Center) in New York City; since 1954 associate pathologist at the Ray Brook State Tuberculosis Hospital, where he died Aug. 31, aged 51, of myocardial infarction and essential hypertension.

Johnson, Jesse Brealand ⊗ Galveston, Texas; University of Texas School of Medicine, Galveston, 1913; professor of radiology at his alma mater; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; past-president of the Texas Radiological Society, and the Galveston County Medical Society; served on the staff of the John Sealy Hospital; died Aug. 18, aged 68, of cancer of the larynx.

Johnson, John Franklin ⊗ Chattanooga, Tenn.; Vanderbilt University School of Medicine, Nashville, 1919; member of the American Academy of General Practice; past-president of the General Practitioners of Chattanooga; died Aug. 31, aged 66.

Joyce, Francis William ⊗ Pittsburgh; George Washington University School of Medicine, Washington, D. C., 1918; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; president of the medical staff and chief pathologist, St. John's Hospital, where he was a member of the staff for many years; died Aug. 21, aged 67, of coronary occlusion.

Kaplan, Isador, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1922; died Aug. 31, aged 65.

Klein, Sidney ⊗ New York City; Columbia University College of Physicians and Surgeons, New York City, 1919; assistant clinical professor of psychiatry at New York University College of Medicine and New York University Post-Graduate Medical School; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychoanalytic Association and the American Psychiatric Association; associated with Hillside Hospital in Glenn Oaks, University Hospital (New York University-Bellevue Medical Center); died July 29, aged 62, of coronary thrombosis.

Kyle, Bernard Hewitt Ⓜ Lynchburg, Va.; born in Buffalo Springs, April 17, 1887; Medical College of Virginia, Richmond, 1911; member of the American Academy of Orthopaedic Surgeons; specialist certified by the American Board of Orthopaedic Surgery; past-president of the Lynchburg Academy of Medicine; veteran of World War I and received commendations from this country and its Allies; a member of the Procurement and Assignment Service for Physicians in World War II and for two years was on the Military Induction Board in Roanoke; designated examiner for the U. S. Employees' Compensation Commission; associated with Marshall Lodge Memorial Hospital, Virginia Baptist Hospital, and Lynchburg General Hospital; orthopedic surgeon for the Norfolk and Western Railway; died Aug. 22, aged 71.

Lacy, Justin Ernest, Knoxville, Tenn.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; an associate member of the American Medical Association; served on the staffs of the Veterans Administration hospitals in various cities; veteran of World War I; died in Washington, D. C., Aug. 28, aged 79, of cancer of the mouth.

McCartney, James Shearer Ⓜ Minneapolis; born in Tarentum, Pa., July 21, 1893; Johns Hopkins University School of Medicine, Philadelphia, 1917; professor of pathology at the University of Minnesota Medical School and the University of Minnesota Graduate School; specialist certified by the American Board of Pathology; member of the American Association of Pathologists and Bacteriologists and the College of American Pathologists; veteran of World War I; served as president of the state board of medical examiners in the basic sciences; consultant in pathology at Abbott Hospital, Asbury Hospital, and the Northwestern Hospital, where he died Aug. 30, aged 65, of cerebral hemorrhage.

McLeod, Alexander Ⓜ Glenallen, Va.; Baltimore Medical College, 1913; veteran of World War I; died in Richmond Sept. 2, aged 67, of cancer.

Mammen, Goeke Henry Ⓜ Chicago; Rush Medical College, Chicago, 1894; fellow the American College of Surgeons; associated with the Lutheran Deaconess Hospital, where he died Aug. 30, aged 86, of uremia and arteriosclerosis.

Mason, Virgil Andrew Ⓜ East Orange, N. J.; Cornell University Medical College, New York City, 1933; certified by the National Board of Medical Examiners; fellow of the American College of Surgeons; associated with the Orange Memorial Hospital, where he died Aug. 21, aged 52, of bronchiogenic cancer with metastases.

Mechling, George Seanor Ⓜ Jackson, La.; born in Newkirk, Okla., Dec. 10, 1905; University of Oklahoma School of Medicine, Oklahoma City, 1932; formerly on the faculty of his alma mater; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists; formerly associated with the Central State Griffin Memorial Hospital and Norman Municipal Hospital in Norman, Okla.; served on the staff of the University Hospitals in Oklahoma City; on the staff of the East Louisiana State Hospital; died in the Ochsner Foundation Hospital, New Orleans, Aug. 22, aged 52, of cirrhosis of the liver.

Merrill, Ralph Edward Ⓜ Glendale, Calif.; Harvard Medical School, Boston, 1920; member of the American Academy of General Practice; on the staffs of St. Joseph's Hospital in Burbank, Glendale Hospital and Sanitarium, Glendale Memorial Hospital, and Behrens Memorial Hospital; died in the Glendale Hospital and Sanitarium Sept. 2, aged 63.

Morris, Hurston H., Portsmouth, Ohio; Marquette University School of Medicine, Milwaukee, 1926; died Aug. 26, aged 62.

Munch, Louise Lucy Ⓜ Chicago; Northwestern University Woman's Medical School, Chicago, 1901; died in St. George Hospital Sept. 4, aged 91, of chronic myocarditis and arteriosclerosis.

Munoz, Roque Narciso Alfonzo Ⓜ Chicago; Chicago Medical School, 1921; veteran of World War I; died in St. Anne's Hospital Sept. 9, aged 65, of acute coronary insufficiency with myocardial infarction.

Murphy, Simon William, Kenosha, Wis.; the Hahnemann Medical College and Hospital, Chicago, 1909; veteran of World War I; died in St. Catherine's Hospital Aug. 31, aged 79.

Myer, Edward Herman, Mahwah, N. J.; Maryland Medical College, Baltimore, 1910; Baltimore Medical College, 1912; died Aug. 22, aged 70.

Osorio, Vasco Eric Monteiro Ⓜ Piedmont, Calif.; University of Louisville (Ky.) Medical Department, 1916; fellow of the American College of Surgeons; veteran of World War I; served with the Army of Occupation in 1919; formerly associated with Queen's, Children's, St. Francis, and Kapiolani hospitals in Honolulu, Hawaii; died Aug. 29, aged 71, of pulmonary embolism.

Pellegrini, Pietro, New York City; Regia Università deglia Studi di Parma, Facolta di Medicina e Chirurgia, Italy, 1896; an associate member of the American Medical Association; associated with Columbus and Italian hospitals and the City Department of Correction; died in Miami, Fla., Aug. 22, aged 87, of acute bronchitis and arteriosclerotic heart disease.

Potter, Marjory Janette Macpherson, La Mesa, Calif.; University of Buffalo School of Medicine, 1897; an associate member of the American Medical Association; died Aug. 16, aged 87, of coronary infarction and cerebral hemorrhage.

FOREIGN LETTERS

BRAZIL

Giardiasis.—Giardiasis is commonly treated with quinacrine, but often this drug produces undesirable side-effects. Rodrigues and Rocha e Silva (*Jornal de Pediatria*, vol. 23, July, 1958) treated 40 children who had this disease with chlorquinaldol. They gave 20 mg. per kilogram of body weight daily for 10 days. If the stools remained positive, they gave a second course using double this dosage. The feces were examined 10 and 20 days after the drug was discontinued. Negative stools were obtained in 29 or 72.5%. There was no intolerance of the drug, even with the larger dose. The authors concluded that the drug should be tried in those patients who showed an intolerance to quinacrine, which cures 90 to 98%.

Biliary Cancer.—Dr. Fernando Paulino and coworkers observed 28 patients (20 women and 8 men) with primary cancer of the biliary tract in the Casa de Saude São Miguel, Rio de Janeiro. The oldest patient was 74 and the youngest 32 (average 54). The tumor was localized in the gallbladder in 18, in the common bile duct in 6, and in Vater's ampulla in 4. Gallstones were found in 18. Microscopy revealed 25 adenocarcinomas, 1 squamous cell carcinoma, 1 scirrhous carcinoma, and 1 adenoacanthoma. Patients who had had gallstones for many years frequently noticed that the character of the pain changed from typical biliary colic to a constant pain in the right upper abdominal quadrant. According to the authors, this was due to neoplastic invasion of the nerves of the hepatic hilus. The results of surgical treatment were disappointing when the tumor was localized in the gallbladder and common duct. In four tumors of Vater's ampulla, duodenopancreatectomy was performed, twice with hope of cure (one patient was still alive two and one-half years after the operation, and the other died with metastases one year and 10 months after operation). Local excision of the ampulla was made in two patients over 70 years old; one was relieved of symptoms for two years. The authors recommend that in all patients with cancer of the biliary tract resection be attempted.

The items in these letters are contributed by regular correspondents in the various foreign countries.

COLOMBIA

First Graduates of New Medical School.—In July the medical school of the Universidad del Valle at Cali held its first graduation. The school, opened in October, 1951, with 60 first-year students as an experiment in medical education, has had a short but important influence on the development of teaching, especially in basic sciences. The new school has been aided by the Kellogg Foundation which financed training in the United States for 13 members of its faculty and gave funds for the biochemical and pathological laboratories. Equipment for the public health and preventive medicine department and the library and training expenses for eight other faculty members were provided by the Rockefeller Foundation. From 1956 a Tulane-Colombia Medical Education Program has functioned under the guidance of Dr. E. C. Faust. The principal objectives of this program in Colombia are (1) cooperation in the planning and revision of the medical courses in undergraduate instruction, including the premedical and clinical years of study, so that future graduates of medical schools will have better training for the practice of medicine, (2) discovery of promising young men interested in teaching medical subjects and recommendation for their graduate training in Tulane University and other institutions, and (3) stimulation of medical research. To implement this program, in addition to a field coordinator, three or four specialists are sent each year from Tulane to work with the seven medical schools of Colombia for periods of three months. Another important contribution of the Valle medical school to the improvement of medical practice in Colombia was the organization of the first seminar on medical education in 1955.

Medical Education.—At the request of Dr. Eduardo Cortés-Mendoza, Dean of the medical school of the National University; Dr. Vernon B. Link, Chief of the Health, Welfare, and Housing Division, United States Operations Mission to Colombia; and Dr. E. C. Faust, a four weeks visit to the Medical school at Bogotá was made by Dr. B. G. Horning in July. His report emphasized organization and administration rather than teaching methods and techniques. The most important suggestions were that (1) the medical school be reorganized into 10 major departments, each representing a broad area of medical education, and that the chairman of each be given a full-time contract, (2) the Hospital San Juan de Dios be reorganized, each department rep-

resenting a broad area of medical education, (3) membership of the school council include the dean, the chairmen of the major departments, and two or more members elected to represent the faculty at large, (4) the deanship be made a full-time position with an adequate salary and secure tenure of office, (5) the dean and council make a more extensive and effective use of committees in the administration of the school, (6) the contest method in the selection and promotion of faculty staff members be discontinued, (7) the preliminary selection of teachers be made by a special committee appointed by the dean with the approval of the council searching the entire nation for the most suitable candidates, (8) the positions of professor and assistant professor be considered permanent until retirement, provided the holders continue to demonstrate growth and ability in their field, (9) the school continue to send brilliant young faculty members abroad for graduate study, especially in basic sciences, and older faculty members for short periods of orientation, (10) each department develop a nucleus of qualified staff members, including the chairmen, (11) adequate salaries be provided for the full-time staff members, (12) the government and the university increase the budget of the medical school, (13) the Junta de Beneficencia hire a well-trained hospital administrator to supervise all of the hospitals administered by it, (14) the Beneficencia de Cundinamarca provide more material help to medical education through the hospitals which it owns, (15) the chief librarian with the help of the library committee develop a plan for assisting medical students to purchase text books, (16) the curriculum be reorganized so that one year would be devoted to premedical studies, five years to medical education, and one year to a supervised internship, (17) "blocks of time" of several hours duration on successive days be allocated to certain of the preclinical subjects so that they may be completed in a shorter period of time, (18) the "block system" featuring the clinical clerkship and bedside teaching be adopted by the clinical departments as soon as possible, (19) less emphasis be placed on lectures and more on group teaching and laboratory work in the preclinical fields and on bedside teaching and the use of the library in the clinical fields, (20) the major emphasis of the curriculum be to provide students with the knowledge and skills necessary for private practice and first level public health positions and as a basis for specialization, (21) preventive medicine and public health be integrated with the curriculum as a whole and the curriculum committee study the amount of time allocated to each basic medical science subject in relation to its importance, (22) a strong department and section of preventive medicine and public health be developed, with adequate staff and facilities, including a modern health center, and a well-developed field area be provided, and (23) graduate medical education programs be developed in the basic sciences and in the clinical fields continuing opportunities for medical education be provided for practicing physicians.

INDIA

Corticosteroids in Tuberculous Meningitis.—K. J. Vyas (*Indian Practitioner* **11**:8 [Aug.] 1958) treated 42 children who had tuberculous meningitis with corticosteroids. Their ages ranged from less than 6 months to just over 5 years. They got 5 mg. of prednisolone by mouth, q.i.d., for one week, followed by 5 mg., b.i.d., for one week, and then 2.5 mg., b.i.d., for another week. In severely ill and moribund patients treatment was initiated by giving cortisone intramuscularly for two to four days followed by prednisolone by mouth. All received simultaneously 0.5 Gm. of streptomycin and 150 mg. of isoniazid daily, irrespective of age and weight, for two months. These doses were later reduced for very young children. Streptomycin therapy was continued for another two months on alternate days and then every fourth day for a further period of two months. Isoniazid therapy was continued for one year.

On this treatment 30 were cured, 8 died, 1 was relieved, and 3 were unrelieved. Of the eight that died, one was 6 months of age, five were between 1 and 2 years old, and two were 4 years old. All but one was admitted in an unconscious or moribund condition. The patient classified as relieved was discharged after two months in the hospital and was much better clinically, conscious, and without neurological defects. Early diagnosis and early institution of treatment are important, but the younger the patient, the worse the prognosis. The results with the use of the hormone were dramatic, some children regaining consciousness in a few days. Most became afebrile promptly and remained so even after discontinuation of the hormone therapy. In a previous series of patients with tuberculous meningitis on whom corticosteroids were not used, 50% died. Thus, the use of corticosteroids definitely improved the prognosis of these patients.

Tropical Eosinophilia.—K. V. Rao treated 40 patients who had tropical eosinophilia with diethyl carbamazine (*Antiseptic* **55**:8 [Aug.] 1958). The age of these patients ranged from 4 to 57 years, most of them being in the second, third, and fourth decade. The daily dosage of the drug was 10 to 12.5 mg. per kilogram of body weight and was administered in three divided doses for 10 days. In children treatment had to be continued for about 15 days to get the same result as in adults. Symptomatic relief was noticed in all but two patients within two days of starting the treatment.

The eosinophil count showed an almost immediate drop, while the lungs were clear of moist or dry rales as early as the third day. No serious toxic effects were met with, only seven complaining of such side-effects as general weakness, giddiness, diarrhea, and rash. The results on the whole were good in 31. In eight recurrence of asthmatic attacks occurred, and in five there was a concomitant rise in the eosinophil count. In three, although the eosinophil count had come down to normal, the symptoms persisted. Roentgenograms of the chest of some were made, and the lungs were seen to have cleared at the end of treatment, when the eosinophil count had also reached normal levels. The most striking features in therapy with this drug were the precipitous fall in eosinophil count immediately after treatment and early symptomatic relief with almost simultaneous clearance of lung signs. Arsenic used in the treatment of tropical eosinophilia also leads to an immediate fall in the eosinophil count, but the symptomatic relief is neither so marked nor so prompt.

Intussusception.—W. Singh and co-workers reported a series of six patients with tumors of the intestine causing intussusception (*Indian J. Surg.* **20**:3 [June] 1958). Benign tumors of the intestine are uncommon and are rarely diagnosed clinically. Intussusception is the most common type of obstruction caused by such tumors. Three of these tumors were hemangiomas and three were fibromas. Two of the hemangiomas were in the small intestine, and the third was in the cecum. One was a single polypoid cavernous hemangioma, and the others were capillary hemangiomas of the small intestine and cecum. The remaining three were fibromas of the small intestine—one with myxomatous degeneration and another with a hyaline change. Five of the six were intraluminal. Three patients had a history of subacute obstruction going on to acute obstruction. The other three had signs and symptoms of acute intestinal obstruction of short duration. A history of previous pain and constipation lasting two months to six years was present in the three with fibroma, one of whom had pigmentation of the skin and subcutaneous neurofibromas. On exploration, intussusception of the ileoileal type was found in four and of the ileocolic type in two. Roentgenograms of four showed dilated coils of small intestine in one and a filling defect or complete obstruction in the others. The appearance was suggestive of intussusception in only two. The authors emphasized the importance of keeping in mind the possibility of finding a benign neoplasm of the small intestine in patients with obstruction, that intussusception is not so uncommon in adults as is usually believed, and that most of the times it is due to a benign tumor.

Pleurisy with Effusion.—P. N. Laha (*J. Indian M. A.* **31**:5 [Sept. 1] 1958) studied a series of 25 patients who had pleurisy with effusion on one side to determine the intrapleural pressure changes on the affected side. The site chosen for measuring the intrapleural pressure was the second intercostal space of the affected side along the midclavicular line, which was above the level of the fluid in all but three patients. On the basis of the findings the patients were divided into five groups. The first included seven whose intrapleural pressure was within the normal range during inspiration and expiration and with regard to mean pressure. This was the first stage of effusion from the point of view of intrapleural pressure. The second group included five whose pressure could be recorded only during inspiration but was within the normal range. If the disease did not stop or improve at this second stage, the third stage set in with further effusion. The normal intrapleural pressure in this stage was modified in such a way as to maintain a negative intrapleural pressure during inspiration but produced a positive pressure during expiration and a mean intrapleural pressure of 0 cm. of water.

The fourth group included three patients in whom the effusion covered the entire pleural cavity. The intrapleural pressure could be recorded only during inspiration and was gradually becoming increasingly positive. The pressure reading during the phase of inspiration was not the correct measure of intrapleural pressure which could not be recorded due to lack of free pleural space. The fifth group included five patients in whom, in spite of the presence of free fluid in the pleural cavity, the intrapleural pressure could not be recorded in either phase of respiration due to obliteration of the pleural cavity above the level of the fluid. The duration of illness, level of the fluid in the pleural cavity, the position of the trachea, and the apex beat did not seem to be correlated with the findings of intrapleural pressure. The factor governing the changes in intrapleural pressure was the amount of fluid collected in the pleural cavity and the consequent collapse of the lung due to its elasticity. A measure of the elasticity of the lung of the affected side was reflected in the intrapleural pressure.

JAPAN

Gumma Fever.—In Gumma Prefecture where a recent typhoon caused severe damage, 1,000 persons were laid low with what appeared to be a new virus infection. The victims were stricken with fever of about 100 F (38 C), acute pharyngitis and conjunctivitis, and diarrhea. Children were first to fall sick, but the disease spread to adults later. The preventive measures advocated include ventilation of dwellings, especially sleeping quarters, and avoidance of gatherings. In Tokyo and Kyoto large numbers

of school children are sick with symptoms strikingly similar to those of Gumma fever. Some health authorities believe this might be a new type of influenza.

Dental Caries.—Along with the census taking of a year ago government dentists made a dental survey of representative populations numbering 30,878 men, women, and children of all classes from various geographical areas and found that 85% of those examined had dental caries. Many were badly in need of dentures. Women with caries outnumbered men by 2%. The incidence in infants and preschool children was high: 17% in one-year-olds; 57% in 2-year-olds; and 80% in 3-year-olds. Among the adults, those requiring major and minor dental treatment exceeded 44%.

SWEDEN

Diagnosis of Silicosis.—Dr. L. Norviit (*Svenska läkartidningen*, July 25, 1958) examined scalene lymph nodes obtained by biopsy from 21 miners whose work might have provoked silicosis. All had been working for many years in an atmosphere of stone dust, and all but one showed radiologically demonstrable changes in the lungs. Before the biopsy, silicosis alone had been diagnosed in eight, silicosis plus tuberculosis in nine, sarcoidosis in one, sarcoidosis plus tuberculosis in one, tuberculosis alone in one, and nothing pathological in one. The biopsy revealed nothing abnormal in eight, sarcoidosis in one, silicosis alone in six, silicosis plus tuberculosis in four, and tuberculosis alone in two. Though biopsy is useful in demonstrating morbid changes in deep-seated lymph glands connected with the lungs, negative findings do not necessarily rule out silicosis.

Guinea Pig Versus Culture Tests for Tubercle Bacilli.—Dr. P. N. Oscarsson, (*Nordisk medicin*, Aug. 21, 1958) studied 3,728 tests carried out between 1950 and 1956 with a view to comparing the effectiveness of the guinea pig inoculation and culture tests for tubercle bacilli. He found that the former gave fewer positive results, the difference being statistically significant with respect to both sputum and gastric washing. With other material such as urine and exudates, the figures were too small to justify any conclusion. The divergencies between the two were most noticeable when only a few bacilli were demonstrable. It must be admitted that neither direct microscopy nor the culture test throws light on the pathogenicity of the germs found, so they may fail to distinguish between tubercle bacilli and nonpathogenic mycobacteria. Oscarsson concluded that the guinea pig test may prove of value as a supplement to culture in certain cases, but for routine examinations the culture test comes first.

Induced Abortions.—With the revision of Sweden's abortion law in 1946 there has been a rising tide of legally induced abortions. In 1951 there were 57 legal abortions per 1,000 live births. Dr. Per Arén studied the events of the past decade insofar as they threw light on what happened to the women involved (*Acta obstetrica et gynecologica scandinavica*, Supplement, 1958). The report deals with the records of 248 women who underwent legal abortion and subsequently again became pregnant, accounting for a total of 389 pregnancies; 100 women who had undergone a legally induced abortion and had subsequently achieved a pregnancy which went to term were selected at random and interviewed. Eighty-four said that, had legal abortion been refused them, they would have let their pregnancies go to term. In none had the subsequent pregnancy and confinement resulted in any threat to their health or working capacity. Another 197 women for whom the legal induction of abortion had been authorized but, for some reason or other, not actually accomplished were interviewed. Subsequent events showed that in 89% the failure to exploit the permission for an induced abortion was fortunate. The author urges a critical revision of the attitude of the community to the interruption of pregnancy on social indications.

Cortisone Treatment of Rheumatism.—The Swedish Ministry of Pensions sends many of its rheumatic patients to a hospital where about 1,400, chiefly suffering from rheumatoid arthritis, were treated in 1956 and 1957. Among them were 323 who had been treated with various forms of cortisone during periods ranging from a few weeks to four years before admission to this hospital. These patients were the subject of a statistical analysis by Dr. F. Bohman (*Nordisk medicin*, Sept. 18, 1958). In 132 there was improvement under cortisone therapy, with a relapse as soon as it was discontinued. In 88 no effect from the drug was observed. In 39 the disease became worse with use of it. In most of these cases cortisone had been given for a prolonged period, with improvement at first followed by aggravation of the symptoms in spite of continuation of the drug. In 41 there had been improvement which was maintained for weeks or months after it was discontinued. In the remaining 23 there was improvement under therapy with cortisone, the administration of which was continued on admission to hospital.

Bohman classified these 323 patients according to the side-effects or complications of cortisone treatment. Of the 91 who showed some side-effects, 39 had psychic disturbances which usually took the form of depression or anxiety. In some apathy and lassitude were the most prominent symptoms. Aggressiveness and dysphoria were also noted. The edema observed in 40 was, in 23, confined to the lower extremities, chiefly below the knee on both sides. In nine the edema was confined to the face

and in eight to both face and legs. Dyspeptic symptoms suggestive of gastritis or peptic ulcer were observed in 23. In eight of these there was radiologic evidence of peptic ulcer. The thrombopenia observed in 12 was never severe, the lowest figures ranging from 149,000 to 193,000. Though there might be some doubt as to a causal relationship between the thrombopenia and the cortisone, no other possible cause of the former could be found in these 12 patients.

Staphylococcic Enteritis and Antibiotics.—Dr. T. Wiklund (*Nordisk medicin*, Sept. 18, 1958) illustrated a discussion of serious staphylococcic infections following the use of broad-spectrum antibiotics with the following case report. A candidate for appendectomy was not operated on because of bronchitis, expectant treatment being adopted with the administration of a total of 3 Gm. of oxytetracycline. On the fourth day of this medication abdominal pain and diarrhea set in, proving refractory to treatment and terminating in death four days later. Cultures confirmed the diagnosis of staphylococcic enteritis, and autopsy revealed a pseudomembranous esophagogastroenteritis. In another patient in whom the lungs had been operated on preoperative and postoperative treatment with penicillin and streptomycin was followed by intractable, fatal enteritis. In a third patient who also died of enteritis, streptomycin had been given by mouth in an attempt to sterilize the digestive tract as a preliminary to a colonic resection. In most such fatal cases of staphylococcic enteritis the blame was put on the broad-spectrum antibiotics given by mouth, but this mishap may also follow the parenteral administration of combined penicillin and streptomycin. The clinical findings are well defined, with abdominal discomfort and diarrhea setting in three to five days after the institution of antibiotic treatment.

UNITED KINGDOM

Homes for the Aged.—It is estimated that by 1977 there will be nearly 500,000 people aged over 75 in Britain. In the last 10 years the number increased by 25% and is now 281,000. The Minister of Health believes that the best place for old people is their own homes. The provision of as many one-bedroom units as possible is needed. Since 1952 the proportion of this type of house increased from 7.5 to 13.5%. The minister has opened a $200,000 home, the first to be built in South Wales specifically for old people. It will accommodate 50 people who will pay between $5.60 and $14 a week for room and board.

Lord Amulree, writing in *Public Health* said few local authorities have interpreted their powers under the National Health Service Act to provide a domiciliary meal service differing from the meals-on-wheels service offered by many voluntary organizations. These are mostly for healthy pensioners. It should be possible, on a medical certificate, for sick or disabled persons to have meals delivered at least five days a week. Many more elderly persons could then be discharged from hospitals.

Lung Cancer Death Rates.—E. C. Hammond, in the *British Medical Journal* for Sept. 13, said that in 1955 the lung cancer death rate reported in England and Wales for men was 2.1 times as high as that reported in the United States and for women 1.6 times as high. A difference of this order of magnitude has existed in male rates for several decades, while prior to 1949 there was only a small difference in the female rates. Among both sexes in the middle-age and old-age groups there are proportionately more cigarette smokers in the United Kingdom than in the United States. On the other hand, at present, the number of cigarettes consumed per smoker per day is higher in the United States than in the United Kingdom. The proportion of male cigarette smokers who inhale appears to be about the same in the two countries. In the United States the average length of the remaining butt after a cigarette is discarded is about 31 mm.; about 5% are 45 mm. or longer, and about 9% are under 20 mm. in length. In the United States in 1957 the main stream smoke of the average cigarette contained about 2.6 mg. of nicotine and 42.8 mg. of tar. More recently, cigarettes with a relatively low content of nicotine and tar have become increasingly popular in the United States.

Current data do not support the hypothesis that a substantial proportion of the difference in lung cancer death rates between the two countries is attributable to differences in the use of cigarettes, but more detailed information on smoking habits and on the chemical composition of cigarette smoke in the two countries is needed before this can be definitely established. In both countries the death rate from lung cancer in smokers as well as nonsmokers is higher in urban than in rural areas. The difference in this respect is far greater between Liverpool and rural areas of Wales than between large cities and rural areas in the United States, but Merseyside (which includes Liverpool) has a higher death rate from lung cancer in men than any other region in England and Wales, so it cannot be considered as typical of the country as a whole. While it is possible that some of the difference in death rates from lung cancer may be due to such factors associated with urbanization as air pollution or occupational exposures, available evidence does not suggest that these factors can account for a large part of the difference. The reported death rate from cancer, exclusive of lung cancer, declined steadily from 1931 to 1956 in England and Wales but rose slightly in the United States during the

same period. Differences in the diagnosis and recording of causes of death may account for a part of the difference between death rates from lung cancer in the two countries.

Health Levy.—A significant pointer to progressive Conservative thought on the National Health Service by Sir Keith Joseph, M.P. for Leeds North-East and joint secretary of the party's Health and Social Security Committees, was reported in the *Daily Telegraph* of Sept. 19. He suggested that there may one day be two levels of Health Service contributions, according to earnings. There will always be a ceiling to the amount that can be spent from taxation. Expenditure above this will have to be financed partly by contributions and partly by charges. As the service grows and improves there may be elements in it that can be charged to patients without discouraging early treatment or unduly burdening the ill. Such charges should be subject to a means test so that those least able to afford payment are exempt. Contributions, too, can grow as average earnings grow, and perhaps there may one day be two levels of contributions: a lower one for those in a lower bracket of earnings and a higher for those above. A graduated contribution, varying with earnings, would have to take personal circumstances into account and would quickly become a second tax system. It would be inexcusable if the government failed to provide essential health services simply because in their view no more cost should be borne by taxation.

The challenge of the next decade is that the Health Service must find some of its own needs by switching some of its present resources and using them even more effectively. Savings and improved value for money expended could be made in the cost of drugs, managerial efficiency, design of hospitals, and improved coordination between hospital, local authority, and voluntary services. So far as drugs are concerned, the greatest saving could be made by reducing the number of prescriptions or the taxborne cost of each one by, for instance, doubling the present charge per item. The time is coming, according to Sir Keith, for new bargain between the community and the general practitioner, a bargain in which the state, by some means, frees the practitioner from the economic incentive to maximize the number of his patients, regardless of the actual constructive treatment he is able or willing to give them. This would be a situation in which the good general practitioner could again earn more than his inferior colleague even though both look after the same number of patients of the same financial status. Some such bargain should emerge, but it will not cost less than now. It will cost more, at least in the short term, though long-term economies by better therapy and better service may emerge. Private practice should be encouraged and more physicians should depend for part of their living on it.

Asian Influenza.—An editorial in the *British Medical Journal* for Sept. 20 stated that past experience has shown that with the appearance of antigenically novel strains of influenza virus earlier ones disappear. Isolations of A virus strains since the Asian strain appeared in 1957 have been almost entirely of this new type. We may therefore expect that viruses closely related to the Asian will dominate the scene for perhaps a decade. In any case the attack of influenza is usually much the same from the patient's point of view. Many physicians will be asked about vaccination. Last year's experience showed that a vaccine made against the current strain and given in time generally diminished incidence by about 67%. The chances of catching influenza are presumably less than they were last winter. It is therefore a matter for personal choice rather than for a country-wide campaign whether, this coming winter, it is worthwhile to get protection from a disease that may not turn up.

WORLD HEALTH ORGANIZATION

Use of Oxygen-15 in Study of Pulmonary Malfunction.—At the Second United Nations International Conference on the Peaceful Uses of Atomic Energy, N. A. Dyson and co-workers (London) stated that the short-lived radioactive isotope, oxygen-15, potentially offers a safe and direct tracer method of studying both the intake of oxygen on inspiration and its clearance by the blood, in small regional volumes of lung. Hitherto, bronchospirometry has been almost the only method of comparing gas exchange in different regions of the lungs, but, since it entails the passing of catheters into the bronchi under local anesthesia so that the gas can be collected it is unpleasant for the patient and the conditions are hardly physiological. Moreover, only a comparison of the whole of one lung with the other is usually practicable. Thus, the use of oxygen-15 marks an important advance. Oxygen-15 is the longest-lived radioactive isotope of oxygen, yet it has a half-life of only two minutes. This short half-life means that a number of tests can be done serially with no residual activity, but it also means that the isotope must be prepared close to the patient. In common with many cyclotron-produced isotopes, oxygen-15 decays by positron emission,

and consequently the annihilation gamma radiation from the lungs may be measured by external scintillation counters. By using pairs of counters connected in coincidence, the volumes examined may be restricted to small cylindrical cores through the lungs.

The results in normal subjects and in patients chosen to represent examples of extreme abnormality of ventilation and blood flow in the lungs were generally as expected. They showed that it is possible to measure the ventilation and clearance by the blood of small volumes of lung with useful accuracy. The ability to discriminate between small areas of lung was good, but the problem of examining a small, localized volume inside the lung (e. g., a cyst) was difficult because normal lung tissue was inevitably included in the field. The chief drawback of the technique as it stands is the poor repeatability of the measurements of clearance rate, and for these it may be necessary to explore parallel counting further with some sacrifice of spatial resolution in order to achieve higher counting rates. The radiation hazard associated with this test, using either parallel or coincidence counting, is acceptable.

Applications of Iodine-132.—At the same meeting K. E. Halnan and E. Eric Pochin (London) stated that iodine-131 has been widely used in the study of thyroid function and is of outstanding value for many clinical investigations. In two important respects, however, an iodine isotope with a much shorter half life, such as iodine-132, offers advantages. The greatest advantage in the use of I^{132} lies in the much smaller radiation doses delivered to the thyroid per microcurie administered, a given oral dose of I^{132} delivering from 1/40 to 1/100 the thyroid radiation received from an equal amount of I^{131}. This reduction in dosage is due not only to the short half-life of I^{132} (2.3 hours or less than 1/80 that of I^{131}) but also to the relatively slow course of radioiodine uptake into the gland from the circulation. In a normal thyroid gland iodine uptake will be only half completed in about six hours, and by this time 85% of the administered I^{132}, but only 2% of I^{131}, will have undergone decay. Repeated measurements of thyroid function after administration of thyrotropic or thyroid hormone may be of value also in certain cases.

Day-to-day tests with I^{132} will readily demonstrate an effect of a single injection of thyrotropic hormone on the normal thyroid or on the thyroid of most patients with hypofunction of the pituitary, but no effect will be demonstrable in patients with primary hypothyroidism. In clinical use it will usually be sufficient to give an injection of thyrotropin immediately after the first I^{132} test and then to repeat the test at the same time a day later. When the diagnosis of thyrotoxicosis is in doubt, it may be valuable to administer thyroid hormone to the patient for one week and then to repeat the I^{132} test, since the normal fall in radioiodine uptake does not occur in the hyperfunctioning gland. It appears therefore that the short half life of I^{132} gives it two substantial advantages over I^{131} both in diagnostic and in research examination of human thyroid function: a reduced radiation dosage to the subject investigated and convenience when repeating tests at short intervals. We have not found its preparation from tellurium-132 to involve any difficulty or hazard sufficient to outweigh these advantages.

Pituitary Ablation by Means of Radioactive Seeds.—At the same meeting Frank Ellis and co-workers (Oxford) stated that they had treated 42 patients who had mammary cancer with widespread metastases by inserting seeds. The results were not impressive statistically, but it must be remembered that all the patients treated had reached the stage when no more benefit could be expected by any other treatment, the possibilities of local irradiation, surgery, and hormone therapy having all been exhausted. Thus, any improvement in the patient's condition was sheer gain, and the considerations to be taken into account were chiefly the risk and discomfort of the operation and the risk and discomfort of complications. The risk of the procedure is small. No patient died as its immediate consequence. The discomfort immediately after the operation consisted chiefly of headache and slight nausea for two or three days and, less constantly, of diabetes insipidus. Of the 42 patients, 15 were improved. Three patients died in less than one week. All these had obvious liver metastases with jaundice and were recognized as deteriorating rapidly at the time of implantation.

Radioactive Gold in the Treatment of Ovarian Cancer.—At the same meeting J. H. Muller (Switzerland) stated that he had treated an unselected group of 51 patients who had ovarian cancer with radioactive colloidal gold (Au^{198}). All of the 10 patients in stage 1, 9 of the 13 in stage 2, 4 of the 10 in stage 3, and none of the 18 in stage 4 were alive and without symptoms after five years. These results indicate that such isotope administration is of definite value since it at least doubled the salvage rate of the ovarian cancer patients with surgically resectable primary tumors.

MISCELLANY

INTERNAL MEDICINE AND THE TRAINING OF INTERNISTS

Paul S. Rhoads, M.D.

Most of the readers of this journal, in rare moments of reflection and self-examination, must have pondered the questions: Of what does the practice of internal medicine consist? What is an internist? Since internists are supposed eventually to be certified by a specialty board, the implication is that they practice a specialized type of medicine. Doubtless, in some suitably remote repository the definition of this specialty lies entombed, but the fact remains that among both the public and physicians themselves there is much confusion as to what is embraced by this most all-inclusive of the specialties.

Some dictionaries sensibly ignore the question. A recent edition of Webster's unabridged dictionary defines internal medicine as, "That branch of medicine dealing with the diagnosis and treatment of diseases of the interior of the body," thus separating its practitioners from, at least, their dermatologic colleagues. "Dorland's Illustrated Medical Dictionary" takes a further step in describing it as "that department of medicine which deals with diseases that cannot be treated surgically," a novel segment of human ills delimited only by the imagination and industry of the surgeons. The same source goes a step further by defining an internist as "A physician who treats diseases of the internal organs," thus slicing off another segment. In Funk and Wagnalls large dictionary the only reference to internal medicine points out that this is a "remedy to be taken internally."

Such definitions obviously will not do. Yet, after several frustrating hours of search in one of America's best-equipped medical libraries, I was able to dig out no good statement of what is encompassed by the term. O. H. P. Pepper,[1] after a long preamble in which the difficulties of such an attempt were set forth, had a try at defining the practitioner of the specialty. "An internist is a physician fitted by sound and applicable knowledge of the basic sciences, a continuing training in internal medicine, a familiarity of fields outside his own, and an intellectual rather than a manual or technical approach, to study and treat the diseases of the field of internal medicine to which he strictly limits himself and to integrate with the knowledge of his own field that of the allied specialities." Dr. Pepper then modestly and truthfully admits that, since "internal medicine" eludes definition, this delineation of the internist is perhaps wide of the mark.

Editorial reproduced from *A. M. A. Archives of Internal Medicine*, October, 1958.

When asked to describe the tasks properly to be undertaken by an internist, I could not compose a definition but had this to say [2]:

> The average patient probably considers the internist a general practitioner particularly interested in diagnosis who has removed from his armamentarium the scalpel, trephine, forceps, plaster cast, and the countless other tools of his craft, confining his own therapeutic efforts to what can be written upon a prescription blank plus the hypodermic needle. This concept may be surprisingly close to the correct one. No specialist can approach in utility to the patient the general practitioner who by incessant study and necessity has mastered the staggering body of medical knowledge and the skills of a dozen surgical specialties required to make him competent to take care of nearly all the needs of those who come to him for help. However, this breed of doctor is almost extinct, for medical knowledge is too diverse and too technical for any one man to acquire all of its essentials.
>
> The "medical man" must strive to come nearest this ideal doctor more than any other of the specialists. It is he to whom the patient may properly turn as having the final word in determining what is the matter and what is to be done. The internist should not operate if a competent surgical colleague is available and usually could not anyway; but he must have enough knowledge of the problems of general surgery, gynecology, obstetrics, otolaryngology, ophthalmology, neurosurgery, genitourinary surgery, and all the other subspecialties so that he will know when surgery is indicated and whom he should call upon for help. Having called in another consultant and concurred in the diagnosis he must accept responsibility for the outcome along with his colleague.

In his delightful essay, "Internal Medicine as a Vocation," [3] Sir William Osler, while regarding internal medicine as a field set apart, wisely refrains from defining it as a specialty. He says in part:

> I wish there were another term to designate the wide field of medical practice which remains after the separation of surgery, midwifery and gynecology. Not itself a specialty (though it embraces, at least, half a dozen) its cultivators cannot be called specialists, but bear without reproach the good old name physician, in contradistinction to general practitioners, surgeons, obstetricians and gynecologists.

He then goes on to point out his own high standards for those to be regarded as internists. Among his recommendations were a 10-year period of "dry bread years" in which were recommended study abroad or at least in other medical centers in this country, some years in general practice, much work with outpatients and without too much preoccupation with "quiz classes" and "journal work." He strongly advised more than passing familiarity with one or all of the disciplines of chemistry, physiology, and morbid anatomy. Of the three, some special knowledge of morbid anatomy was considered most essential for the clinician.

It is obvious that the composite of "internal medicine" cannot be neatly encompassed by a definition. There are just as obviously widely differing opinions as to the kind and amount of training required by those who wish to be internists. To some this dilemma may appear to be of purely academic importance. To others, who after five years of postgraduate preparation are about to take Board of Internal

Medicine examinations, the question is practical and urgent. Upon their estimate of what, in the minds of the Board examiners, makes up the body of facts and skills which the internist should have for minimum equipment can depend success or failure in the Board examinations. Without going into the question of whether one who fails in the examination can or cannot be as effective an internist as one who passes, the fact is that unsuccessful candidates for Board certification are for the most part denied recognition as capable consultants. Admission to many hospital staffs and medical societies, advancement in academic rank in medical schools, and other privileges are denied to them. Members of the Board have from time to time deplored this practice of making differentials in emoluments and promotions contingent on Board certification, but the practice is here, and young internists know they had better get Board certification. One of the kindest and wisest of the Board chairmen gave the admonition that "the responsibility of acquiring knowledge rests with the candidate and the responsibility of maintaining the standards of knowledge required for certification rests with the Board." [4] In the long run, however, the future of internal medicine depends largely not upon what each person thinks should make him a good internist but what the Board collectively thinks.

Up to now, there has been little to criticize in either the personnel or the decisions of the Board of Internal Medicine. From the outset, thoughtful conscientious men have tried to lay down rules rigid enough to assure quality in the product of the training programs but flexible enough not to cramp the individual interests of the candidates in these all-important years of their development.

In 1940 Dr. Irons [5] quoted from the brochure of the Board:

> The American Board of Internal Medicine does not propose to establish fixed rules for the preliminary training of candidates for certification in this field. Broad general principles for training, however, may be outlined—"A sound knowledge of physiology, biochemistry, pharmacology, anatomy, bacteriology and pathology as they apply to disease is essential for continued professional growth of the individual who practices internal medicine. Such knowledge may be acquired in a number of ways. These include sciences closely integrated with clinical facilities, and service in well organized clinics or in preceptorships."

No one can question the desirability of such emphasis on the nonclinical disciplines or the wisdom of the declaration to keep the program very flexible, and yet time spent in a preceptorship part of the original program [6] is now unacceptable to the Board and for very understandable reasons.

There are differences of opinion as to what constitutes "sound knowledge" of the nonclinical subjects listed above. Some members question whether one year in one or more of these branches is enough—certainly there can be no prolonged special training in all of them. Others question the value of even a year of research experience as an integral part of the training of a resident. Lewis [7] feels that above all else an internist must have the capacity to make a thorough physical examination and to take a good history and make a penetrating analysis of it. In his view two years is too little time to develop in most of the candidates the broad knowledge of medicine and clinical skills that are required of internists. He thinks only those with more than average interest and aptitude for research should be required to participate in it. "If we are to do our job as I see we should do it, we will have to take an almost heretical course and decide that we will train some of our apt young men to become expert clinicians and clinical teachers and others to be investigators."

These points are well taken. The Board has made a real effort to make the program for qualification flexible enough to adapt itself to the special circumstances of physicians who have prepared themselves as specialists in internal medicine in a variety of ways. Plan H, the one most recently adopted, makes it possible for a man committed particularly to research and academic medicine to spend the two required postresidency years chiefly in the laboratory, provided he keeps his hand in clinical medicine by work in the hospital wards or dispensary once a week. Such men must be specially recommended for this privilege by the professors of medicine in the schools which they serve.

Whether other young internists not aiming for teaching careers but with strong research interests could not similarily benefit from two years with more emphasis on research and less on "practice" is a question that must be answered on an individual basis.

Dr. Irons, in his discussion of Board examinations points out that the written questions are so designed as to test the powers of the candidates to come to proper conclusions after certain clinical data are stated rather than to delve too deeply into their factual knowledge. In grading, more attention is given to logical deductions than to "right answers." Such emphases in evaluating the examinees are praiseworthy but difficult of attainment. Even more difficult, but much more important at this stage of a young man's development, is the evaluation of intangibles. In other words, what kind of a doctor should be encouraged to enter the field of internal medicine?

1. Is he impulsive or does he have the patience for long hours of continued study and for careful but monotonous tasks in the laboratory?

2. Does he have the conviction that *every* patient is important and worthy of his help whether he can pay for it or not?

3. Does he have sustained enthusiasm? Will he willingly undertake the painstaking preparation required to make him a good teacher?

4. Does he have enough devotion to his job to look up what he doesn't know, to make house calls, to get up at night when needed?

5. When called upon for a consultation will his efforts be devoted to helping his colleague to do what is best for the patient or to impressing the patient?

No one will deny the importance of such intangibles, yet how can an examining Board make such evaluation?

No Board can make rules which will answer all of these special problems of the peculiar division of medicine occupied by the internists, and yet a recognition of the problems suggests some changes that might help.

The present steps being taken by investigating committees from the College of Physicians to learn more about what makes up the residency program in the various approved hospitals should prove most constructive. If carried on perceptively it could furnish some indication of what the various internists in charge of residency programs consider important and of the way these ideas are implemented. More important, some evaluation of the teachers themselves could be had.

From an interchange between teachers in the various hospitals and the Board more minds could be brought to focus on the problem of arriving at some clearer definition of the minimum body of knowledge and skills which should reasonably be required of all internists. Perhaps an examination devised to test a candidate's grasp of the "fundamentals" so agreed upon could be given at the end of the three-year residency program. Successful candidates could then go about the next stage of their "dry bread" period pursuing their particular fields of interest in a more relaxed frame of mind.

Only those who have seen young men "sweat out" the year or two before their examination frantically reading textbooks and journals in the hope of cramming in enough facts in all the fields of internal medicine to satisfy the examiners can be aware of the anxiety produced in them. Few persons will question the value of high standards and the necessity of examinations to maintain them. However, could not these two or three years be spent more usefully if a candidate could be assured that the decision regarding his certification would be made on the basis of such points as the following?

1. Consideration of a comprehensive report on his performance by certified internists and faculty members of medical schools to whom the candidates had been assigned for guidance and supervision. From these reports would come information on the "intangibles."

2. Demonstration of the ability to take a good history, make a good physical examination, and make logical conclusions and recommendations after reviewing the laboratory data on one or two patients chosen at random.

3. Demonstration of a fairly good grasp of fundamental knowledge of internal medicine as a whole plus more complete knowledge in the field of his special interest, such as cardiology, metabolic diseases, or infectious diseases.

Implementing of Point 3 would require assignment of candidates to examiners, some of whom would have special interests in the same field as those of the candidate. In case of disagreement in evaluation by two examiners, a third should be called in before a candidate is failed. At this stage of a man's training the psychologic impact of failing is too devastating for the decision to be reached with any hint of haste or unfairness. If an unfavorable verdict is reached, and inevitably this will happen in many cases, the candidate should be entitled to a consultation with members of the examining board for counsel as to how his deficiencies might best be remedied or whether or not he should change direction.

It should be pointed out again that I have the highest admiration for every one of the present members of the Board of Internal Medicine and a profound appreciation of the difficult task they face.

In friendly discussions various members sharply disagree with some points brought up here—on perfectly reasonable grounds. However, since our specialty has special problems not faced by more narrow ones, a full discussion of the manner in which its practitioners are to be trained seems to be in order. The public should be assured of a quality product. On the other hand, care must be taken not to cramp the development of young men of imagination and unusual initiative by insisting on a too rigidly standardized training program.

References

1. Pepper, O. H. P.: What Is an Internist? Ann. Int. Med. **13**:1791 (April) 1940.

2. Rhoads, P. S.: Your Future in Internal Medicine, J. Student A. M. A. **4**:38 (Nov.) 1955.

3. Osler, W.: Essay—Internal Medicine as a Vocation, in Aequanimitis, with Other Addresses to Medical Students, Nurses and Practitioners of Medicine, ed. 2, Philadelphia, P. Blakiston's Sons & Co., 1922.

4. Schnabel, T. G.: American Board of Internal Medicine, J. A. M. A. **152**:1590 (Aug. 22) 1953.

5. Irons, E. E.: The American Board of Internal Medicine After 4 Years, Ann. Int. Med. **14**:146 (July) 1940.

6. Bierring, W. L.: The American Board of Internal Medicine, Ann. Int. Med. **10**:1746 (June) 1937.

7. Lewis, H. P.: A Look at the Future of Internal Medicine, J. A. M. A. **158**:1414 (Aug. 20) 1955.

BUSINESS PRACTICE

This is the fifth in a series of excerpts from the brochure on the Business Side of Medical Practice, prepared by the American Medical Association in cooperation with the Sears-Roebuck Foundation.

FINANCING THE ESTABLISHMENT OF AN OFFICE

Setting up a medical office requires money—specific outlays for rent, equipment and furnishings, and possibly some remodeling, as well as enough to cover the doctor's living expenses during the practice-building period.

A physician is usually considered an excellent credit risk, but banks generally are not permitted to make unsecured loans. In the beginning, then, it may be wise to turn to the companies who outfit doctors' offices. Such companies will often help him finance his office if properly approached. The physician's first job is to appraise his actual financial needs over a period of several months, taking stock of his own reserves.

His financial evaluation sheet might include items like these: (1) cash on hand—income from part-time job as insurance examiner during first six months of practice, estimated income from practice during first six months; and (2) needs—first and last month's office rent, minor office alterations, office furniture, cost of instruments and equipment, cost of basic office supplies, stationery, cards and business records for office, estimated utilities, telephone charges at start, cost of necessary licenses and permits, estimated living expenses for first few months, including operation of car, and insurance.

Balancing his assets against his estimated expenses will give the new physician a rough idea of his financial needs. He will be in a better position to approach the people who can provide the necessary capital armed with facts and figures. His worst mistake would be to misrepresent his needs or current financial situation.

The companies which sell a physician equipment, supplies, and furniture are usually most liberal in extending credit and liberal payment terms. Some items of equipment, such as an x-ray unit, can be rented until the doctor can afford to buy one.

The physician should make a get-acquainted call on the president or an officer of the bank and state his intentions of opening an office. He can explain why he chose this particular community, announce his intentions of opening an account with the bank, and establish friendly rapport. If he does need a loan, the doctor's approach should be direct and business-like rather than apologetic. He is not asking for a favor but is presenting a business proposition. Prepared to lay all his cards on the table, the doctor is in effect saying: "Considering these facts, how much can you lend me?" If the banker is "sold" on the physician as a risk and the proposition outlined, he probably will lend all the law permits. A physician who makes his problem so interesting that the banker becomes interested in helping him solve it will fare well.

If a doctor still has need for additional funds, there are other sources he can investigate. He can check private loan companies or call on prominent citizens in the community he has selected, using the same approach he used on the banker. It is always easier to raise money in the community where he plans to practice. However, at this point a word of caution must be injected. Do not try to get everything at once if it involves an overload of debts. It is sometimes best to plan ahead for what seems to be a present need than to buy just because you can get it on credit.

Protecting Your Credit

Only the physician himself can protect his credit. Credit is based on confidence—faith in the person to whom it is extended. It is no sin to be in debt, but the doctor should clear up his indebtedness as soon as possible. Here are tips on guarding credit:

1. In paying all obligations, interest payments come first.

2. Pay all commercial bills promptly when due. If this is impossible, make a personal call on the store's credit officer, explain why payment is impossible, and tell him when it can be paid.

3. Because a physician cannot estimate monthly income at the start of his practice, it is best to make arrangements for repayment of the entire amount of a bank or personal loan at some specified date rather than on a monthly basis. Three to six months are customary time limits on unsecured loans, but notes can be renewed. Keep a calendar showing date of expiration for each note, and, if it cannot be repaid then, arrange to renew before it becomes due.

MEDICAL FILM REVIEWS

From the Heart of Town: 16 mm., color, sound, showing time 13 minutes. Produced in 1958 by William J. Ganz Company, New York, for E. R. Squibb and Sons, Division of Olin Mathieson Chemical Co., New York. Procurable on loan or purchase ($35.50) from American Red Cross, 1730 E St. N. W., Washington, D. C.

This film depicts the visit of a bloodmobile to a typical American town and demonstrates that community-level cooperation is essential to the success of the blood program. It tells of a community's preparation for and response to the visit of the bloodmobile and also shows how scientific research is developing the "prescription for life," including such blood products as gamma globulin, serum albumin, and fibrinogen and also the methods for obtaining, handling, storing, and processing whole blood. On the whole, this is a good film. Especially important is the section which deals with the various uses of the blood. Another important point which is brought out clearly is that industry also donates its services through research. The photography is very good. This film is recommended for use in local organizations, such as churches, civic groups, and schools in communities which are organizing a program of this kind.

A Career in Bacteriology: 16 mm., color, sound, showing time 15 minutes. Produced in 1957 by and procurable on loan ($5.50) or purchase ($150) from Audio Visual Center, Indiana University, Bloomington, Ind.

The purpose of this film is to develop an interest in bacteriology as a vocation, to show the studies in bacteriology pursued by college students, and to present the various vocational opportunities for those who study bacteriology. By photomicrography it shows protozoa, algae, molds, yeast, and bacteria, and by animation it shows the minute size of bacteria and their rapid rate of reproduction. Some of the actions of micro-organisms in the cause of and treatment for diseases, in the maintenance of soil fertility, and in the production of food for humans and food supplements for livestock and poultry are pointed out. This film aims primarily at making the profession of the bacteriologist attractive to the senior high school student and the college student in his first or second year before he has made up his mind about the choice of a career. It will also be of interest to the physician who is asked to speak on careers in the medical and health field. It may be of interest to the nurse, medical student, and public health worker. On the whole, it is well done technically and is correct factually.

NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

Breech Delivery: 16 mm., color, sound, showing time 18 minutes. Prepared in 1955 by Professor Bruce Mayes, University of Sydney Department of Obstetrics, Sydney, Australia. Procurable on loan (service charge $3) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film demonstrates the types of breech presentation, relation to pelvic types, diagnosis by palpation, and x-ray; x-ray pelvimetry; and external version. Breech extraction is then demonstrated using Lovsett's technique to deliver the arms. This is a good teaching film which does not utilize any living person. Breech extraction is demonstrated on the obstetric manikin, and a stillborn, slightly macerated fetus is shown. For this reason, some persons might object to the film, and it is not recommended for showing to nurses. It embraces good general principles and is highly recommended for showing only to audiences of physicians.

You Are There: The Discovery of Anesthesia: 16 mm., black and white, sound, showing time 25 minutes. Produced in 1956 for CBS Television. Procurable on rental or purchase ($135) from McGraw Hill Book Co., 330 W. 42nd St., New York 36, or on loan ($2) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This is a dramatic and exciting presentation of the facts surrounding the discovery of anesthesia. Although certain small freedoms were taken with facts in order to make a more dramatic and pictorial presentation, in general, this is a very accurate portrayal of the early days of the discovery of anesthesia. One gathers from this picture that Crawford Long performed surgical anesthesia prior to Wells and Morton. Yet, he did not give this discovery to the world. There can be little doubt, however, that he deserves a place in the early discoverers because of his prior use of surgical anesthesia. That Wells had utilized anesthesia successfully in dental cases prior to Morton's surgical discovery on Oct. 16, 1846, is brought out in the film but somewhat slighted, as is the work of James Young Simpson. The place that Morton plays in the discovery of anesthesia is well portrayed. There can be little doubt but that this man, so beautifully portrayed in this movie, really gave anesthesia to the medical profession. This film is an excellent digest in portraying the discovery of anesthesia and is suitable for lay audiences, medical students, interns, residents, nurses, and the allied professions. The sound, photography, and over-all dramatic presentation are excellent.

19
V.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Clinical Reconstruction of the "Bangungut Syndrome." J. B. Nolasco. J. Philippine M. A. 34:371-376 (June) 1958 [Manila].

The term "bangungut syndrome" had been coined to cover the typical signs and symptoms and the postmortem findings in young Filipinos who died suddenly during sleep after a heavy meal; "bangungut" is the Tagalog word for nightmares, which was chosen from common usage for convenience and not from agreements with the common belief that nightmares caused these unexplained deaths. The author reports the case of a 27-year-old man with bangungut syndrome, who, unlike the patients reported on previously, was able to tell some of his subjective feelings and who was subjected to at least a cursory physical examination before he died. A few hours before admission this patient had convulsive seizures, with groaning, lasting for several minutes while he was asleep. On regaining consciousness, he complained of epigastric pain, nausea, and salivation and was taken to hospital. On admission, the heart sounds were weak, the pulse imperceptible, the blood pressure was zero, and the pupils were symetrically dilated. Shortly after being placed in bed the patient had convulsive seizures, with transient cyanosis, groaning, rolling of the eyeballs for one minute followed by relaxation of the body, pallor, a short heaving respiration, and then apnea. Artificial respiration was applied, but the patient died.

With the clue given by this patient, the author began to be on the lookout for patients coming to the hospital at night with complaints referable to the respiratory, central nervous, circulatory, and digestive systems. Thus, the cases of 2 men and 2 women, between the ages of 17 and 51 years, were collected, which were considered to represent early stages of the bangungut syndrome. Two of these patients had nightmares; all of them had difficulty in breathing. One patient, a medical student, noticed decreasing pulse volume and rapid pulse; another had hypotension and tachycardia; the remaining 2 patients showed normal blood pressure levels, but their blood pressures were determined several hours after the attacks. Three had symptoms referable to the central nervous system, such as heaviness of the head, numbness, or loss of consciousness. Retinal edema was observed in one. All the patients gave a history of having previously eaten preserved fish or foods which have been considered as "bangungut-genic." A brother of one also had nightmares after eating the same food as the patient. Thus, the clinical features of the bangungut syndrome, so far detected, are as follows: The patient has eaten preserved fish or fish products; the acme occurs while the patient is asleep; manifestations may progress to death or may completely disappear within 24 hours; the respiratory, central nervous, circulatory, and digestive systems are the organ systems usually involved.

Aregenerative Anemia Associated with Benign Thymoma. B. Clarkson and D. J. Prockop. New England J. Med. 259:253-258 (Aug. 7) 1958 [Boston].

The authors present the histories of 2 patients in whom aregenerative anemia was associated with benign thymoma and point out that 14 cases with this syndrome have been described before. The suggestion that the association of thymoma and aregenerative anemia was not a matter of chance was first made by Humphreys and Southworth in 1945, when they found that cure of the anemia followed removal of the tumor. Thymectomy has been performed on 8 of 9 patients with the combination of thymoma and aregenerative anemia described since then, but the results of thymectomy have been far from uniformly successful. Only 1 of these 8 patients was cured, and 2 others obtained some alleviation of their anemia. One died within 24 hours of operation, and the other 4 had no apparent benefit from the operation. The 2 patients presented here likewise derived no benefit from the resection of the thymoma. One of the 2 patients is unusual in that the thymoma was removed 2 years before the development of the anemia.

No therapy, other than blood transfusions, was of benefit in patient's not responding to thymectomy, except perhaps splenectomy and corticotropin therapy in 2 patients. An extract prepared from the thymoma in one of the patients was infused intravenously for 10 days into a dog that had pre-

---

The place of publication of the periodicals appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individuals in continental United States or Canada who subscribe to its scientific periodicals. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover 1949 to date only, and no photoduplication services are available. No charge is made to members, but the fee for others is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

viously been given acetylphenylhydrazine to induce an anemia and erythroid hyperplasia. No inhibition of erythropoiesis was produced by the thymoma extract. The establishment of the true relation between thymoma and aregenerative anemia will require further studies on patients who have this combination. If normal erythropoiesis had developed after thymectomy in their second case, the authors had planned to attempt to reproduce the anemia by injecting an extract of the tumor. This should probably be tried when further patients are found who are benefited by removal of the tumor.

Giant-Cell Granuloma of the Respiratory Tract (Wegener's Granulomatosis). E. W. Walton. Brit. M. J. 2:265-270 (Aug. 2) 1958 [London].

The author reports on 7 men and 3 women, between the ages of 33 and 75 years, with a syndrome characterized by symptoms of progressive ulceration in the respiratory tract, together with signs of widespread inflammatory disease to which the name "Wegener's granulomatosis" has been applied by other workers. Forty-six additional cases of this syndrome in 26 male and 20 female patients, between the ages of 12 and 70 years, were selected from the literature. Two groups were distinguished as follows: In the first group of about 40 patients, persistent purulent rhinorrhea was accompanied by nasal obstruction and crusting, antral pain, and epistaxis. Otorrhea, deafness, or ulceration of the gums were the initial symptoms in a few of these; later rhinorrhea occurred in each. In the second and smaller group, attention was drawn to the lungs because of chronic cough, hemoptysis, or pleurisy. Often the constitutional upset was out of proportion to the apparent intensity of the local lesion, and the patients sought advice because of persisting malaise, fever, or weakness. The course was usually rapid, progressing to death in 5 months, on the average, and occasionally in 4 weeks. Five of the 56 patients had a more chronic illness, with periods of remission and survival up to 4 years. Though temporary improvement sometimes followed antibiotic treatment, the local lesion always persisted. Spread of the inflammatory process led to extensive mucosal ulceration and cartilaginous or osseous destruction in the nose and palate of the patients in the first group, and to widespread pulmonary consolidation in those in the second group. Sooner or later signs of widespread inflammatory disease, such as fleeting arthralgia, numbness and tingling in the extremities, sensory loss, muscle weakness or paralysis, and a hemorrhagic vesicular rash, most frequent on the skin of the face, wrists, and elbows, and the oral mucosa, occurred in all the patients. On roentgenologic examination, the lungs of 38 patients showed dense circular or oval opacities in one or more lobes, often with central cavitation, and varying in size up to that of a hen's egg. Less often bronchopneumonic infiltration was the only notable change.

The basic pathological features were giant-cell granulomatous ulcers at one or more levels in the respiratory tract; the ulcers involved the nose and paranasal sinuses in 34 patients, palate and pharynx in 21, tongue in 7, larynx in 14, trachea in 17, and bronchi in 23. In addition to the ulceration of the respiratory tract, widespread giant-cell granulomas and necrotizing lesions of small vessels were observed. The characteristic round or oval consolidations in the lungs were not infarcts but conglomerate areas of peribronchial necrosis. The kidneys were severely affected in all but 3 patients; enlargement and blurring of the architecture were the usual macroscopic changes, and focal "fibrinoid" necrosis of glomerular loops and periglomerular granulomatous inflammation were almost constant microscopic findings. The disease is clearly a separate entity, differing both clinically and in the character and distribution of the lesions from similar conditions, such as polyarteritis nodosa and malignant granuloma. It begins as a progressive ulceration of unknown causation in the respiratory tract. Sooner or later widespread lesions, the result of a hypersensitivity reaction, complete the aspect of the disease. Treatment should be primarily directed toward healing of the initial lesion, and radiotherapy proved to be successful in some cases, with control of secondary infection by suitable antibiotics. Administration of cortisone or other steroids is the treatment of choice, once widespread lesions have occurred.

Precirrhosis: Its Clinical Entity. E. Aron and P. Jobard. Arch. mal. app. digest. 47:849-860 (July-Aug.) 1958 (In French) [Paris].

Cirrhosis is characterized by a structural derangement of the liver caused by extensive generalized fibrosis. Exact classification of the various stages of the disease is based on the anatomic appearance of the liver, but for the practitioner cirrhosis may be regarded as either a hypertrophic or an atrophic process leading to failure of hepatic function, hemorrhage, ascites, and edema. Hepatologists who have studied the cirrhotic process distinguish 2 stages in its early development: (1) alcoholic precirrhosis, which comprises all forms of alcoholic hepatitis, steatotic and cytolytic, in which the 3 histological elements characteristic of cirrhosis (a zone of cellular atrophy, hyperplastic nodules, and sclerosis) are present in varying combinations and to varying degrees, and (2) beginning alcoholic cirrhosis, in which the cirrhosis is clearly established. Obvious alcoholic cirrhosis in its later form, when it can be diagnosed on the basis of the clinical findings without recourse to laboratory studies, should be regarded as a terminal stage of

the disease. Distinction between the precirrhotic and cirrhotic stages is not always easy; systematic examination of the liver in alcoholic patients often reveals histological evidence of anatomic cirrhosis, which cannot be confirmed either by the clinical signs or by the results of biological tests. Similarly, the histological aspect of the liver does not always indicate the subsequent course of the disease. Thus, simple steatosis may be associated either with a minor clinical state or with a course of the utmost gravity. This absence of parallelism between the histological and biological findings, on the one hand, and the clinical symptoms, on the other, which was evident in many of the 166 alcoholic patients admitted to the authors' service in 1957, is discussed in greater detail on the basis of 9 illustrative case reports.

The data presented suggest the advisability of regarding all enlargements of the liver in alcoholic patients as precirrhotic, keeping in mind, however, the important fact that enlargement of the liver is not always present in these patients. Alcoholic precirrhosis should not be neglected or dismissed as commonplace; on the contrary, it should be regarded as an extremely serious condition which has an unpredictable course and which must be treated promptly and energetically. Prompt treatment, with complete elimination of alcohol, in the precirrhotic period, which may extend over many years, is, in fact, the only way to prevent the development of cirrhosis.

Carcinoma of the Colon under the Age of 40. J. A. Ezzo, J. F. Sullivan and R. E. Mack. Ann. Int. Med. 49:321-325 (Aug.) 1958 [Lancaster, Pa.].

Of 840 patients with pathologically proved carcinoma of the colon, who were admitted to the St. Louis University Hospitals between January, 1950, and May, 1957, 32 (19 men and 13 women) were under the age of 40 years. Twelve of them, who were between the ages of 23 and 39 years, had carcinoma of the rectum. Eight of these patients died 3 to 58 months after the diagnosis. The remaining 4 patients were alive and well 5 to 24 months after the diagnosis was made. The remaining 20 of the 32 patients had carcinomas of other portions of the colon than the rectum. One patient could not be followed up and is presumed to be dead. Thirteen patients died within 3 to 28 months after they had been seen. Two patients are alive but have metastatic disease 6 and 24 months after the onset, and 1 patient is alive 6 months after operation for a ruptured carcinoma of the cecum. The remaining 3 patients are alive and well 1 to 4 years postoperatively. Thus, of a total of 32 patients with malignant tumors of the colon, 25 are dead or fatally ill. Seven patients are living without disease 5 to 48 months postoperatively. If one presumes that these 7 patients will live 5 years or more, the very best the 5-year survival rate can be is 21.7%.

It is difficult to explain the very poor prognosis in this group of young patients. Their symptoms, including melena, pain, constipation, diarrhea, and weight loss, had been present for the same period of time as in the older patients. Surgery was not unduly delayed in any patient. As a group these patients were better operative risks than their older counterparts, and, although operative mortality rates reported by other workers have generally been quite high, varying from 3.0 to 9.6%, there were no operative deaths in this series. The absence of lymphatic or vein invasion at the time of surgery was of little prognostic value. Two patients who had had no evidence of spread at surgery died of metastatic disease within one year. This observation confirms Dukes's statement that lesions of the rectum give rise to metastases more rapidly in young patients than in those who are older. Carcinoma of the colon apparently has an accelerated course in patients under 40 years of age.

Chronic Adrenocortical Insufficiency (Addison's Disease). A. M. de Andino Jr. and J. Pérez Cruet. Bol. Asoc. méd. Puerto Rico. 50:163-170 (May) 1958 (In English) [Santurce].

Chronic adrenocortical insufficiency either is idiopathic or is caused by tuberculosis of the adrenal gland and, more rarely, is due to bilateral tumoral metastases, leukemic infiltration, amyloid disease, hemochromatosis, or histoplasmosis. The disease is characterized by malaise, fatigability, gastrointestinal disorders, loss of weight, progressive anemia, low blood pressure, dizziness, a weak heart, severe prostration, bronze-like pigmentation of the skin, mental disorders, and loss of the sexual function. The disease is either congenital or acquired. The congenital type is seen in premature infants whose mothers have had deficient adrenocortical secretion; the infants die in the neonatal period. The disease of the acquired type may be transient, such as that which follows administration of steroids for a prolonged period, or it may be primary and complicated by tuberculosis or other chronic infection.

The authors report the first proved case of chronic adrenocortical insufficiency in a Puerto Rican woman, 48 years old. The symptoms were typical and had lasted for 8 months when the patient reported to hospital. The patient was given cortisone, 200 mg., Cortate, 10 mg., and an intravenous drip of 1 liter of 5% dextrose in isotonic sodium chloride solution. The maintenance treatment consisted of a daily dose of cortisone, 20 mg., of Cortate, 4 mg., and of sodium chloride, 8 Gm. The treatment was continued for 3 consecutive weeks, discontinued for 3 weeks, given for 2 weeks, discontinued for 3 days, and again given, a dose of 12.5 mg. of cortisone being administered for 2 more weeks. The

treatment of pulmonary tuberculosis was started immediately upon the patient's hospitalization and was continued throughout the treatment for chronic adrenocortical insufficiency. It consisted of the administration of isoniazid in daily doses of 300 mg. and of streptomycin in daily doses of 1 Gm. At the end of 3 months of hospitalization and treatment, the symptoms of adrenocortical insufficiency had disappeared. The patient gained 26 lb. in weight. She was transferred to a hospital for tuberculous patients for further antituberculous treatment.

The Serum Protein Picture in Gastroduodenal Ulcer. R. Dupuy and A. Beaune. Semaine hôp. Paris 34:1979-1982 (July 18-28) 1958 (In French) [Paris].

Published data on protein metabolism in patients with ulcer have been reviewed, together with the authors' own observations on 36 patients. It appeared, in spite of some contradictory findings, that abnormal serum protein levels were present in all the patients with gastroduodenal ulcer. This abnormality affects either the total protein level or the various protein fractions or, concurrently, one protein fraction and the total protein level. Moreover, the serum protein picture does not seem to be influenced by antalgic drugs during the acute stage of the ulcerative disease. The protein picture of the patients was abnormal, not only during periods of acute pain but also during periods of remission, during which it was characterized by great instability. The transition from a period of remission to an acute stage of the ulcerative disease is apparently accompanied by an increase in the disturbances in the serum protein level. The changes observed in the serum protein values differed in patients belonging to different ethnic and geographic groups, but whether these differences are due to ethnic or to nutritional or climatic influences is not now known.

Influence of Protein Therapy on the Serum Protein Picture in Patients with Ulcer. R. Dupuy and A. Beaune. Semaine hôp. Paris 34:1983-1986 (July 18-28) 1958 (In French) [Paris].

The occurrence of abnormalities in the serum protein picture in patients with duodenal ulcer during periods of painful exacerbation, previously reported by the authors, has been confirmed by further studies. These changes can be corrected, at least partially, by intravenously administered protein. The 36 patients studied were given protein in the form of peptones in 30 intravenous injections distributed over 30 or 60 days, as required in each case. The results were verified by a standard procedure, consisting of 3 determinations of the serum protein level at certain intervals: the first, before treatment; the second, 5 to 10 days after the beginning of treatment; and the third, at the end of treatment, i. e., 30 or 60 days after the first examination. Treatment brought about a decrease in elevated serum protein values and an increase in those that were reduced. As a general rule, the serum albumin level, which was increased at first, decreased steadily from the beginning to the end of treatment, usually reaching nearly normal values. The serum globulin level, which was normal at the beginning of treatment, increased during the first days of treatment and then returned to the initial value. These variations in the serum albumin and the serum globulin level led during the first phase of the treatment to a significant decrease in the albumin-globulin ratio; the ratio might later increase slightly, but in any case it would settle down at the end of treatment to a level that was nearly normal and was lower than it was in the beginning. By contrast, the serum protein titers in patients with ulcer do not seem to be corrected by various other treatments, such as gastric fomentations or the administration of protein hydrolysates or vitamin or atropine compounds.

The mechanism by which protein therapy acts to produce changes in the serum protein picture is not yet clear, but the indications are that the peptones have an anti-inflammatory effect and that they also act specifically on the reticuloendothelial system. Further study will be needed to clarify these points and to establish the extent to which protein therapy may be regarded as a specific treatment for duodenal ulcer.

Adrenal Hypofunction After Corticoid Withdrawal. A. Vermeulen. Acta endocrinol. 27:321-330 (July) 1958 (In English) [Copenhagen].

Since the introduction of such potent synthetic glucocorticoids as prednisone and prednisolone, the incidence of adrenocortical hypofunction has increased. These steroids are at least 4 times as active in depressing adrenocortical activity as similar doses of cortisone. In view of these facts the author investigated the reactivity of the adrenal cortex to exogenous corticotropin, after a prolonged period of prednisone or prednisolone therapy, by the daily determination of urinary 17-hydroxycorticoids. All 25 patients were treated with prednisone or prednisolone according to various dosage schedules. During the treatment they all received a weekly intramuscular injection of 20 I. U. of corticotropin. Eleven patients had rheumatoid arthritis, 5 had acute rheumatic fever, 1 had infectious mononucleosis, 1 had ulcerative colitis, and 7 had bronchial asthma. Prior to hormone administration the adrenocortical function of the patients was assumed to be normal.

The author found that adrenocortical hyporesponsiveness to stress is frequent after prolonged treatment with prednisone or prednisolone, as shown by the low 17-hydroxycorticoid excretion after corticotropin stimulation. This hypofunction

of the adrenals may persist for months after corticoid therapy has been stopped, and situations of stress, such as severe infection and major operation, may prove fatal because of acute adrenal insufficiency. Weekly injections of corticotropin during prolonged prednisone or prednisolone therapy do not seem to prevent this adrenal hyporesponsiveness, and a few injections of corticotropin at the end of the treatment are not sufficient to prevent this adrenocortical insufficiency. The author recommends that each series of treatment with prednisone or prednisolone be terminated by giving corticotropin for 5 or 7 days together with prednisone or prednisolone in decreasing doses and then administering corticotropin alone for 3 days. This seems to reduce the risk of hypocorticalism.

SURGERY

Surgical Ascariasis in Children: A Review of 50 Cases. N. Fernando. J. Trop. Pediat. 4:61-70 (Sept.) 1958 [New Orleans].

Obstruction has been the commonest surgical complication of ascariasis, the condition usually commencing with vomiting, often after the administration of a vermifuge. In the 50 cases reviewed, 28 of the children had been given a vermifuge a few days prior to admission. Associated with the vomiting was colicky abdominal pain, mild at the onset but gradually increasing in severity and localized to the umbilicus. The child often vomited roundworms and had constipation, and in the more advanced cases there was abdominal distention with visible peristalsis. An ill-defined sausage-shaped mass lying transversely across the lower abdomen, more often to the right, was found. In the majority of these malnourished children the worms could be palpated through the abdominal wall, and the lump of worms was often disclosed at rectal examination.

That obstruction is at least partly mechanical is shown by the longitudinal disposition of the worms along the length of the intestine, twisted very much in the fashion of ropes. The worms, whose natural habitat is the upper part of the small intestine, may partially or completely obstruct the lumen of the intestine, may vary from a few to several hundreds in number, are often twisted tightly upon themselves, and may thus be propelled onwards along the intestine like a sausage or foreign body. The obstruction may be partly due to spasm of the intestinal muscles, caused by the irritation and reaction of the chitin from the outer covering of the worm's body on the intestinal mucosa of the host, or the introduction of a purgative or vermifuge may cause the worms to secrete a toxic fluid which will initiate the spasm. Although rare, intussusception can be caused by the roundworm, and 4 such examples were encountered in the present series. Volvulus caused by the Ascaris parasites is rare and often fatal, 3 such cases being described in this series. In acute obstruction with peritonitis at operation, a perforation with ascarides in the peritoneal cavity is frequently found. However, no perforations were found associated with obstruction in this series, although a search was made in 4 cases. In the remaining 24 cases a perforation was found in either the appendix, the jejunum, or the ileum. It is of note that many examples have been reported where no perforations were detected, although live roundworms were found in the peritoneal cavity.

The presence of an Ascaris infection in the various organs produces no pathognomonic pattern. Since the small intestine is the habitat of ascarides, the commonest symptoms are referrable to this viscus and vary from vague epigastric distress, nausea, or vomiting to the severest excruciating abdominal pain of perforation or obstruction. There may be associated systemic manifestations, such as anemia, fever, malnutrition, anorexia, lassitude, insomnia, urticaria, headache, and, rarely, convulsions. The diagnosis depends on the identification of the ova or the worms in the feces. Two methods are commonly employed in the treatment of obstructions: (1) manual disengagement of the Ascaris bolus without enterotomy, and milking the worms into the cecum by gentle manipulation; and (2) enterotomy with evacuation.

Tracheotomy for Treatment of Postoperative Respiratory Insufficiency. J. Wassner and H. L'Allemand. Chirurg 29:342-345 (Aug.) 1958 (In German) [Berlin].

The authors report on 32 surgical patients on whom tracheotomy was performed to prevent postoperative respiratory insufficiency or to combat manifest respiratory acidosis. Of the 32 patients, 12 had injuries of the cranium and brain, 5 had been operated on for cranial injuries, 3 had operations on the neck, 1 had an abdominal operation, 9 had undergone thoracic surgery, and 2 had tetanus. Eighteen patients died; death resulted from the primary disease in 14, tracheotomy was performed too late on 2, and 2 were beyond help. Fourteen patients survived. These data show the high incidence of respiratory insufficiency, particularly after injuries of the cranium and brain, in which unconsciousness and a deficient peripheral circulation resulting from impairment of the brain stem favor the development of pneumonia.

Respiratory insufficiency is always a danger to be kept in mind when additional damage is sustained by lungs already handicapped by emphysema, asthma, or the rigidity of the thorax in older patients. Such additional respiratory embarrassment consists of loss of mobility of the diaphragm, painful trauma of the thorax, serial rib fractures,

or unilateral and bilateral pneumonia after cranial trauma and barbituric acic poisoning. Rest in bed as such may bring on this condition in patients with asthmatic bronchitis. Tracheotomy should be considered in all patients in whom the occurrence of respiratory insufficiency is suspected. When performed too early in doubtful cases, tracheotomy will not be harmful. Indications for tracheotomy depend on clinical experience rather than on special laboratory reports. The authors are convinced that the number of surgical patients who may be helped by tracheotomy is not small. In certain cases in which tracheotomy alone is insufficient, it should be supplemented with artificial respiration.

Prognosis in Patients with Carcinoma of the Stomach. H. Denck and F. Helmer. Chirurg **29**:289-294 (July) 1958 (In German) [Berlin].

The authors report on 1,429 patients with carcinoma of the stomach who were admitted to the second surgical clinic of the University of Vienna between 1933 and 1955. The tumor was located in the fundus or at the cardia in 25.4% of these patients. It was possible to perform resection in 43.2%. Sixty-five per cent of the patients with carcinoma of the antrum had operable lesions as compared with only 44% of those with carcinoma of the body of the stomach and 39% of those with high location of the tumor. The duration of the disease and the age of the patient at the time of the operation had no effect on the operability. The primary operative mortality rate within the first 4 postoperative weeks was 21.5%, with 16.8% after partial resection according to Billroth 1 and 2 operations, 33.6% after total gastrectomy, and 32.5% after resection of the cardia. The operative mortality rate in the patients between the ages of 20 and 39 years was 7.4%; in those between the ages of 40 and 59 years it was 16.3%; and in those between the ages of 60 and 80 years it was 27.2%. The operative mortality rate was 14.3% in patients with carcinoma of the antrum, 22% in those with carcinoma of the body of the stomach, 33.5% in those with carcinoma of the cardia, and 31.5% in those in whom the entire stomach was involved. These figures represent the average for a 22-year period. Since 1951, as a result of the use of antibiotics and modern methods of combating shock, the primary operative mortality rate was reduced to 11% after Billroth 1 and 2 resections, to 29% after total gastrectomy, and to 23% after resection of the cardia.

Of 463 patients who were discharged after radical gastric resection, 43 were lost to follow-up; 67.5% of the remaining 420 patients were still alive after 1 year, 46% after 2 years, and 36% after 3 years, while the 5-year survival rate was 28%. The 5-year cure rate in all the patients with carcinoma of the stomach admitted to the clinic was 8.5%. The life expectancy thus can be extended by surgical treatment to 5 years or longer for hardly 10% of the patients. The term "wide resection" was applied to a resection area in which the tumor was at a distance of more than 3 cm. from both the resection margins (histologically), and the term "limited resection" was used for other resection areas. Three years after a wide resection, 40% of the patients were still alive, and 32.5% were alive after 5 years; the corresponding figures for the limited resection were 28 and 19% respectively. Consequently, the broadest possible resection in healthy tissue is required.

In contrast to the general assumption that the prognosis is particularly unfavorable in young patients with carcinoma, the survival time was not shorter among younger patients who underwent resection than among those of more advanced age. Although the chances for a permanent cure are becoming better after a 5-year survival, the possibility of recurrence of carcinoma still remains even after a longer postoperative interval, and several such cases were observed. The higher mortality rate among patients with a shorter preoperative duration of their disease than among those with a longer duration does not suggest a better prognosis for a patient with carcinoma of long preoperative duration; rather the prognosis is better for one with a slowly growing carcinoma for which he may consult a surgeon only late. A 5-year survival was obtained by 26% of those who underwent resection for carcinoma of the antrum, by 37% of those with resection for carcinoma of the body of the stomach, and by only 13% of those with resection for carcinoma of the cardia. The more favorable prognosis in patients with carcinoma of the body of the stomach appeared to be statistically significant. The prognosis also appeared significantly more favorable in patients with carcinoma of the polypoid-cauliflower types than in those with infiltrating tumors. The life expectancy was considerably reduced in patients with lymph node metastases, even if it seemed that macroscopically the metastases were radically removed. Routine cytostatic treatment after radical surgical intervention and cytostatic therapy after intentionally performed palliative resection in selected patients are recommended in order to improve the results of surgical treatment and with these the prognosis for those with carcinoma of the stomach.

Problems of Acute Cardiac Arrest and Its Treatment. K. Spohn and E. Kolb. Chirurg **29**:346-352 (Aug.) 1958 (In German) [Berlin].

Cardiac arrest occurred in 5 of 15,521 patients operated on at the surgical clinic of the University of Heidelberg in 1956 and 1957, i. e., an incidence of 0.032%, or 1 case of cardiac arrest in 3,104 surgical interventions. Of the 5 patients, 3 were men, between the ages of 31 and 57 years, operated on

for bronchial carcinoma, stenosis of the aortic valves, and hydrops of the gallbladder, respectively, and 2 were women, aged 51 and 56 years, operated on for benign pyloric stenosis and cancer of the breast respectively. The man with aortic stenosis and the 2 women died.

In the first male patient, in whom cardiac arrest occurred twice at short intervals in the course of pneumonectomy for bronchial carcinoma, electrical defibrillation was successful both times with the first electrical impulse. Spontaneous rhythmic action with sufficient performance was immediately restored. Reflexes originating in the hilus were the main cause of ventricular fibrillation, and the favorable course resulted from the early diagnosis of the cardiac arrest in the open thorax and its rational treatment. The second male patient died in the operating room; there was extreme hypertrophy and also dilatation of the left ventricle, and its blood perfusion was deficient due to the severe aortic stenosis and inadequate coronary circulation. Electrical defibrillation became effective only with the third electrical impulse, but the resulting spontaneous action remained insufficient because of the high degree of hypoxia of the myocardium caused by the intracardiac manipulation and temporary obturation of the aortic valve by the surgical instruments. In the third male patient fibrillation occurred before the operation was started. Some time elapsed before the diagnosis was made and the heart was exposed. Hypoxia had developed in the myocardium, and defibrillation was successful only after several electrical impulses and after intensive intrapericardial massage. The favorable course, despite the relatively long duration of ventricular fibrillation in this 31-year-old patient, was explained by the predominantly functional factors which elicited the arrest.

In the first female patient who underwent gastrectomy, treatment of cardiac arrest consisted exclusively of transdiaphragmatic cardiac massage. Action of the heart was restored by a mechanical stimulus (the clamping of a vessel onto the diaphragm), suggesting hyperexcitability of the autonomic nervous system; the presence of an asystole was assumed. Pulling on the ligamentum hepatogastricum, and on the mesentery very likely, were the reflex-eliciting events, since the arrest immediately followed these manipulations. In the second female patient an initial total atrioventricular dissociation with insufficient ventricular performance turned into asystole. Intravenous administration of arterenol and epinephrine was ineffective. An attempt at transthoracic administration of electrical impulses failed. Only then were thoracotomy and cardiac massage performed, but the asystole no longer responded to therapy and the patient died.

These observations confirm the experiences of other workers that ventricular fibrillation can be controlled easier than asystole. Defibrillation was possible in all 3 patients with ventricular fibrillation, and morphologic reasons were responsible in 1 of them in whom the restored spontaneous action remained insufficient. Of the 2 patients with asystole, circulation could be restored in only 1, but interruption of the cerebral circulation, although of short duration, with the resulting severe irreversible impairment, caused the death of this 56-year-old patient.

NEUROLOGY & PSYCHIATRY

Encephalitis Caused by Asian Influenza. D. Furtado. Rev. neurol. 98:192-205 (No. 3) 1958 (In French) [Paris].

The author reports the case of a 21-year-old soldier who served at an air force base near Lisbon, Portugal, where the entire military personnel had been attacked by an epidemic of Asian influenza. This soldier, like all his comrades, had fever, cough, and catarrhal symptoms at the onset of his illness, but from the onset he also had a marked disturbance of consciousness and spasms of the muscles acting on the jaws. He had 2 generalized convulsions on the second day of illness and was admitted to hospital in status epilepticus. His blood pressure was somewhat low, and he sweated profusely. The extremities were flaccid; the reflexes of the upper extremities were weak, and those of the lower extremities were abolished. There was papillary edema of the right eye. Auscultation revealed severe bronchitis. Treatment with phenobarbital, chlorpromazine (Largactil), and tetracycline was instituted, and lumbar puncture was performed. The next day the patient had no convulsions but was in stupor. The temperature which was 39.5 C (103 F) at onset remained high, and the bronchitis became worse. On the 5th day the stupor deepened, the temperature rose to 40 C (104 F), and death occurred after another epileptic attack.

Autopsy on this patient revealed a hemorrhagic tracheobronchitis, diffuse foci of hemorrhagic bronchopneumonia, and some hemorrhagic foci in the ventricular septum of the heart. Microscopic examination of the central nervous system showed lesions in the main portion of the brain, particularly in the protuberance and in the central nuclei, and less severe lesions in the cerebral cortex and the cerebellum. These lesions consisted of dilatation and congestion of all the vessels, including also the capillaries. Hemorrhagic foci were observed in the parenchyma adjacent to the vessels. The vessel walls were inflamed, and there was infiltration of the Virchow spaces and perivascular edema. The ganglion cells and nerve fibers were affected. There was also extensive infiltration by mononuclear, hematogenous, and glial cells. The leptomeninges were congested and inflamed.

There was no biological proof that Asian influenza had caused this patient's encephalitis, since the virus had not been isolated from him. Yet the clinical presumption was extremely strong, since the patient belonged to an epidemic center with several hundred cases and the Asian variety of influenza, type A, virus had been isolated from some of the patients. The autopsy findings in this patient of hemorrhagic tracheobronchitis and small diffuse foci of bronchopneumonia with a tendency to hemorrhage were exactly the same as in other patients who had died of the influenza. The conclusion that the case was one of severe influenza associated with diffuse and fatal encephalitis, therefore, seemed to be justified. The extensive and early involvement of the nervous system in this patient is suggestive of a direct attack of the influenza virus on this system, similar to that observed in patients with Japanese B encephalitis, rather than of an allergic process so often held responsible for such cases.

Negative Bacteriological and Serologic Results on Reexamination of Problem of Mycobacterial Etiology of Multiple Sclerosis. H. Bauer, K. Bonitz and V. A. Salchow. Medizinische, No. 29/30, pp. 1128-1132 (July 26) 1958 (In German) [Stuttgart, Germany].

In an attempt to reexamine the concept that multiple sclerosis is a mycobacterial disease, the authors carried out a bacterioscopic study for acid-fast bacteria in the cerebrospinal fluid obtained from 17 patients with multiple sclerosis. The precipitate obtained by centrifugation of the cerebrospinal fluid of these patients was used for culture experiments on various mediums and also for inoculation into guinea pigs. In none of these patients was it possible to demonstrate mycobacteria pathogenic to man or animals or saprophytic mycobacteria. In 2 specimens of cerebrospinal fluid, rod-shaped acid-fast structures were observed microscopically, but culture and animal experiments carried out with these specimens gave negative results.

Serologic studies, including complement-fixation reaction, flocculation reaction, hemagglutination, and hemolysis, were performed on 79 persons, 58 of whom had multiple sclerosis and 21 served as controls. The evaluation of the combined results of these studies with regard to tuberculosis revealed positive findings in 7 of the 58 patients, doubtful findings in 7 others, variable findings in 3, and negative findings in 41. Findings were positive in 1 of the 21 control persons, doubtful in 2, and negative in 18. The absolute frequency of positive and doubtful results obtained in patients with multiple sclerosis and the comparative results obtained in control persons do not permit drawing conclusions concerning a mycobacterial causation of multiple sclerosis.

Further Studies of an Epidemic of Exanthem Associated with Aseptic Meningitis. D. A. J. Tyrrell, R. R. Lane and B. Snell. Quart. J. Med. 27:323-333 (July) 1958 [London].

The authors report an epidemic of a febrile disease with headache, which involved 85 patients seen between September and November, 1956, in a practice covering about 3,500 persons in a mixed mining and rural area near Sheffield, England. There were only 8 adult patients, and nearly all the others were children, less than 10 years of age; parents and children were affected in 12 families. Many patients had a maculopapular rash, lymphadenopathy, aseptic meningitis, and lesions of the buccal membrane, either separately or in combination. Vomiting was a common initial symptom, and some adults complained of myalgia. The disease was benign, but convalescence was sometimes rather long. Thirty-three strains of the virus were isolated, and rising antibody titers were revealed by 3 separate methods in 10 of 14 patients. Similar studies of control patients gave negative results. The virus was associated with all forms of the disease and probably caused it. The isolated strains of the virus were of identical type and were related to Coxsackie, group A, viruses and enteric cytopathogenic human orphan (ECHO), type 9, virus. The same virus was recovered in similar cases in many parts of the Western world at about the same time. The authors have proposed the term "benign exanthematous virus meningitis" for this syndrome.

Influence of Temporal Lobectomy on the Mental Condition of Patients with Psychomotor Epilepsy. T. Alajouanine, J. Nehlil and R. Houdrat. Rev. neurol. 98:165-171 (No. 3) 1958 (In French) [Paris].

The authors report on 22 patients with psychomotor epilepsy who underwent temporal lobectomy performed with the aid of electrocorticography; the pole of the temporal lobe was removed and the excision extended in depth to the cornu Ammonis and, if possible, to the amygdaloid nucleus. In 18 of the 22 patients the psychomotor epilepsy was associated with mental disorders; 3 of these had mental debility and were, therefore, excluded; of the remaining 15, 7 had severe mental disturbances, and 8 had minor mental disturbances. The 7 patients with severe mental disturbances were divided into 2 groups, one including 4 patients with manifestations of depression and the other including 3 patients with severe character changes associated with violent impulsion. Of the 4 patients with depression, the manifestations in 3 were not improved by the operation, but in 1 the depressive tendency was considerably improved; the irritable and unbearable patient became quiet and euphoric and appeared to be surprised himself that he had been impatient and depressed; he was able to re-

sume his activities. The patients with severe character changes associated with violent impulsion were those who benefited most from the operation. One of them no longer had the compulsive urge to chastise the interrogator or to take possession of a car and drive away at maximum speed. Another who had constantly terrorized his parents and siblings with his persecution complex and suicide threats was completely transformed; he was quiet and able to work like a normal person. A child whose compulsive urges had led to acts of violence against his family and schoolmates was able to lead a normal life within the family. The 8 patients with minor mental disturbances underwent temporal lobectomy not for their mental troubles but for their refractory psychomotor seizures. The seizures of these patients improved considerably, and so did their psychic behavior. Although there was no strict parallelism in all the 15 patients between the effect of the lobectomy on the psychomotor seizures and on the associated mental disturbances, as a rule those patients whose psychomotor seizures were most favorably influenced by the operation also showed the most definite mental transformation. These observations suggest that in psychomotor epilepsy severe mental disturbances are a strong indication for surgical treatment.

First Poliovirus Isolations Done in Hawaii: Preliminary Report. C. K. S. Yuen, W. H. Civin and P. Y. Tamura. Hawaii M. J. 17:537-538 (July-Aug.) 1958 [Honolulu].

The authors report on 6 boys and 7 girls, between the ages of 9 months and 5 years, in 12 of whom a diagnosis of paralytic poliomyelitis and in 1 of "aseptic meningitis" was made clinically. Of the 13 patients, 8 had not been vaccinated; 1 had received 1 Salk vaccine injection, 1 had received 2 injections, and 3 had received 3 injections. Type 1 poliomyelitis virus was isolated with the aid of cell cultures at the Queen's Hospital tissue culture laboratory in Honolulu from the stools of all 13 patients. The clinical diagnosis of poliomyelitis was thus confirmed by isolation of the virus.

Cerebrospinal Fluid Neuraminic Acid Deficiency in Schizophrenia. S. Bogoch. A. M. A. Arch. Neurol. & Psychiat. 80:221-227 (Aug.) 1958 [Chicago].

Neuraminic acid is a normal constituent of the gray matter of the brain, in which it occurs in combination with carbohydrate and lipid substances in the form of a macromolecular brain ganglioside. The authors studied the presence and the concentration of neuraminic acid in the cerebrospinal fluid obtained in routine diagnostic and anesthetic lumbar punctures from 195 patients, including 29, between the ages of 20 and 63 years, with schizophrenia, 19 adult mental patients without schizophrenia, and 147 patients in a general hospital. Seventy-two of the 147 patients were children less than 7 years of age, 29 were children between the ages of 7 and 15 years, and 46 were adults. The method employed for the determination of neuraminic acid in the cerebrospinal fluid obtained from these patients is described, with the precautions to be observed. The mean neuraminic acid content of the cerebrospinal fluid obtained from patients with schizophrenia was considerably below that obtained from adults without schizophrenia and comparable only to values found in some children less than 7 years of age.

The presence of neuraminic acid in the cerebrospinal fluid, its association with the proteins of this fluid, and the observed variations in concentration suggest that there may be, in addition to the classical concept of a fixed-brain barrier function of brain ganglioside, a circulating component associated with antibody functions. The tendency for the concentration of neuraminic acid in the cerebrospinal fluid to increase with age in man suggests that this substance may be involved in maturation processes in the nervous system. The failure of chemical maturation shown by the schizophrenic patients would correlate meaningfully with clinical evidence showing a failure in psychological maturation. Thus, if the function of the barrier-antibody system is the maintenance of a selective environment for the brain, then the failure of this system could account for the disorganization which is manifest in the psychotic state. The possession of an inadequately developed barrier-antibody system would represent a specific vulnerability to psychosis. In addition to experiments designed to test barrier functions in patients, it will be of some interest to determine the effect of the administration of neuraminic acid itself and of neuraminic-acid-containing substances on psychotic patients.

GYNECOLOGY & OBSTETRICS

Early Diagnosis of Tumors with Particular Reference to Carcinoma of the Uterus. A. P. M. Cappa. Minerva med. 49:2200-2219 (June 2) 1958 (In Italian) [Turin, Italy].

Vaginal and cervical smears for the purpose of detecting carcinoma of the cervix were taken routinely on 712 women, who were employed in 2 factories. Smears were stained by the methods of Papanicolaou, Feulgen, and Unna-Pappenheim. Cytological examination was followed by karyological, and the latter by circular biopsy if the repeated findings of the immediately preceding method were suspicious or positive. Circular biopsy, which was done on 51 women, confirmed carcinoma of the cervix in 20 women and left 3 suspicious cases unresolved. Intraepithelial carcinoma was present in 6 patients, early invasive carcinoma in 4 and invasive carcinoma in 10. It would have not

been possible to detect carcinoma in 8 patients on the basis of the clinical findings alone. Positive findings by cytological and karyological methods were subsequently reversed by histological method, which thus gave negative response for carcinoma in 31 patients. However, negative findings by cytological and karyological methods were subsequently reversed by histological method, which gave positive interpretation for carcinoma in 2 patients. The average age of the patients with preinvasive and early invasive carcinoma was 37.9 years and that of the patients with invasive carcinoma was 49.8 years.

PEDIATRICS

Is Interstitial Plasma-Cell Pneumonia Caused by One of the Adenoviruses? O. Vivell and G. Lips. Ztschr. Kinderh. 81:181-182 (No. 2) 1958 (In German) [Berlin].

Morphologically identical changes in the form of inclusion bodies were observed in the pharyngeal epithelium in patients with "colds," presumably caused by adenoviruses, and in young infants with interstitial plasma-cell pneumonia. It was suggested that there might be an etiological connection between these 2 diseases. A common complement-fixation antigen is one of several characteristics of the adenoviruses. Since a complement-fixation test was available also for interstitial infantile pneumonia, the authors investigated whether the cause of interstitial plasma-cell pneumonia in infants might be related to the adenoviruses. They did not find antibodies against adenoviruses in 17 infants with interstitial plasma-cell pneumonia, who had high complement-fixation titers against a pulmonary antigen from a fatal case of interstitial pneumonia. Only 3 of 23 patients, with antibody titers in the adenovirus complement-fixation test, had a positive complement-fixation test also for interstitial plasma-cell pneumonia. Of 29 children in a children's home in which interstitial pneumonia was endemic, 7 had positive reactions to interstitial pneumonia and 8 to adenoviruses. Only one child had positive reactions to both. The authors conclude that the cause of interstitiial plasma-cell pneumonia in infants does not belong to the group of adenoviruses.

Cardiac Infarction in a Fetus. D. Schuler. Arch. franç. pédiat. 15:647-652 (No. 5) 1958 (In French) [Paris].

The author reports the case of a hemorrhagic infarct of the myocardium in a fetus. The mother was in labor for 3 hours when admitted to the obstetric clinic of the University in Budapest, Hungary. She had hypertension, edema, and albuminuria. Examination revealed 2 fetuses, one in vertex presentation and the other in transverse presentation. Intrauterine death had occurred in the latter. The living fetus was delivered spontaneously. Ten minutes later an artificial rupture of the bag of the dead fetus was carried out, a podalic version was done, the fetus was extracted, and autopsy was performed. The body of the dead fetus was covered by a sebaceous coat. Punctiform hemorrhages were observed at the level of the portion of the pleura lining the upper lobe of the left lung. The heart was of grayish-red color and was somewhat flaccid. At the anterior surface of the left ventricle and encroaching on about half of its posterior surface, there was a definitely demarcated area of more firm consistency and dark red color, which projected by a few millimeters into the anterior surface of the right ventricle. A similar area formed a margin at the anterior border of the interventricular septum. The same discoloration also was observed at the apex of the heart, and it continued toward the base of the heart, ending at a distance of about 1 cm. on the side of the atrioventricular groove. These changes were perceptible throughout the entire thickness of the myocardium, with the exception of some uninvolved areas at the level of the left ventricle and of a subendocardial layer. Some punctiform hemorrhages located under the epicardium were observed in the right ventricle and on the posterior surface of the left ventricle. A hemorrhage, the size of a finger pad, was observed adjacent to the atrioventricular branch of the left coronary artery, in the posterior portion of the left ventricle and next to it. There were no other abnormal alterations of the heart; the coronary arteries particularly were normal. A hemorrhage, the size of an infant's fist, was observed under the dura mater at the level of the occipital and temporal lobes. There was a rupture of the vena cerebri magna (vena galeni) and a tear in the dura mater covering the left portion of the cerebellum. These findings suggested that the myocardial infarction was the result of a coronary spasm, which itself was elicited by trauma of the central nervous system and by toxemia.

Staphylococcus Empyema in Children. C. C. J. Sia and S. C. Brainard. Hawaii M. J. 17:339-344 (March-April) 1958 [Honolulu].

The authors report on 8 children, between the ages of 3 weeks and 2 years, who were admitted to the Kauikeolani Children's Hospital in Honolulu for empyema. Staphylococcus pyogenes var. aureus was isolated from the pleural fluid of these patients. Most of them had a history of infection, such as measles or upper respiratory disease, for which they had been given penicillin and broad-spectrum antibiotics. A few days later there was usually a sudden spike in fever, with dyspnea, and the patients appeared toxic; cyanosis, dyspnea, and shock were present on admission of the 3-week-old

patient. All the patients were severely ill on admission and had grunting respirations, poor color, and temperatures usually above 102 F (39 C). Chest findings were those of a consolidating process involving one or more lobes of the lungs, with dulness and diminished breath sounds. Paralytic ileus was a common finding after hospitalization. Leukocytosis varied from 17,000 to 35,000 leukocytes per cubic millimeter, with a "shift to the left" in all the patients.

Medical treatment consisted of administration of erythromycin, chloramphenicol, novobiocin, and large doses of aqueous penicillin. Combinations of the 4 drugs were generally selected. Oxygen and intravenously administered fluids were given. Gastric decompression was required in the youngest infant to combat the paralytic ileus. General supportive measures included blood transfusion, antipyretic therapy, and positioning the patient on the involved side. Needle aspirations of the lung were done from 1 to 5 times. The amount of fluid removed varied from a few to 70 cc. Closed drainage was performed in 3 patients, and open rib resection and drainage in 2. The 3-week-old infant had a fulminating course and died. The other 7 patients recovered completely, although complications, such as bronchopleural fistula with pyopneumothorax/ and encapsulated pulmonary abscess, occurred. Hospitalization varied from 17 to 30 days.

Early diagnostic pleural taps and intercostal tube drainage are recommended. An attempt should be made to follow the important principles in the treatment of empyema, with early control of infection, evacuation of the pleural space, and reexpansion of the lung. Frequent chest roentgenograms offer an excellent guide to therapy. Chloramphenicol, erythromycin, and novobiocin are the most effective antibiotics at the present time. With a combined medical and surgical approach, one may hope to have a low mortality and morbidity.

Investigations on the Etiology of Plasma-Cell Pneumonia in Infants. L. Moser. Ztschr. Kinderh. **81:** 152-157 (No. 2) 1958 (In German) [Berlin].

The author attempted to isolate the causal factor of interstitial plasma-cell pneumonia in infants by means of tissue culture techniques. Lungs of 12-to-14-day-old chick embryos served as the primary culture medium. The tissue cultures revealed intracellular processes that resembled the nuclei of thrombocytes or of pneumocystis carinii. Observation under the fluorescence microscope revealed that these forms were living cells or parts of cells. It is highly probable that these forms are not the cause of interstitial plasma-cell pneumonia, but rather they are autogenous cell products which, like thrombocytes under certain conditions, play a part in the defense mechanism. In this connection the author mentions reduced thrombocyte counts in rats with vitamin A deficiency and profuse formation of thrombocytes in the endothelial cells of the subcutaneous lymph nodes after the administration of large doses of cod liver oil. Review of the literature revealed that some investigators had called attention to the fact that large doses of vitamins had been given before interstitial plasma-cell pneumonia became evident.

The pneumocystis carinii-like forms are not characteristic for one definite disease entity but have been found in various species of animals and in human cadavers. That interstitial plasma-cell pneumonia is an infectious disease is proved by the fact that it can be transmitted, by the complement-fixation reaction and by the isolation of the virus. The successful tissue culture of the virus and its identification by the complement-fixation and neutralization tests is to be described in a later report, but a photomicrograph in a 1200-fold magnification is reproduced. It is suggested that the virus is a large one and seems to belong to the group that includes the viruses of psittacosis and pneumonitis.

DERMATOLOGY

Evaluation of the Clinical and Serological State of 416 Well Treated Neurosyphilitics After Long Term Observation. F. Kalz and A. Scott. Acta dermat.-venereol. **38:**155-167 (No. 2) 1958 (In English) [Stockholm].

The authors report on 490 outpatients with neurosyphilis who were treated at the syphilis clinic of the Royal Victoria Hospital in Montreal, Canada, between 1936 and 1949. Only 74 patients (16%) were lost to observation. Of the remaining 416 patients who were followed for a period ranging from 7 to 20 years, 30 had general paresis, 47 taboparesis, 63 tabes dorsalis, 86 meningovascular neurosyphilis, 156 asymptomatic neurosyphilis, and 34 congenital neurosyphilis. In the first years of the study most of the patients received fever therapy followed by, or combined with, the administration of pentavalent or trivalent arsenic compounds. For a period of 2 years artificial fever therapy in conjunction with the administration of penicillin was used. In the last 10 years, penicillin alone in doses of 10 million units was given routinely, usually 2 or 3 weekly injections of 900,000 units, for a period of 3 to 5 weeks. An attempt was made to assess the prognosis of these well-treated patients with regard to the normalization of the spinal fluid changes, the alteration of the clinical symptoms throughout the observation time, their working capacity, social integration, the causes of death, and their life expectancy.

The average time for normalization of the spinal fluid was 13 years; a positive reaction of the blood to the Wassermann test in low titer persisted in 71

patients and in about 5% the total protein level remained elevated in the absence of any signs of cerebrospinal fluid activity or clinical progression. In all but 3 patients the acute inflammatory phase responded to therapy; 3 patients required retreatment with very large doses of penicillin. The final clinical outcome was satisfactory in 40 (52%) of 77 patients with general paralysis of the insane and taboparesis. The outcome was unsatisfactory in 17 patients (20%), while the remainder showed an initially satisfactory response to treatment, on which psychological disturbances and eventual deterioration were later superimposed. The treatment results in the 110 patients with tabetic symptoms were not satisfactory; while progress of the disease was arrested and the atactic symptoms improved in most of these patients, shooting pains persisted in most of them. The end-results of treatment in the group of patients with meningovascular neurosyphilis were very satisfactory, except in those in whom irreparable brain damage due to cerebral thrombosis had occurred. A considerable number of patients with asymptomatic neurosyphilis had unspecific symptoms including tiredness, loss of appetite, insomnia, and occasional headaches, which could have been easily misinterpreted as neurotic complaints; these symptoms disappeared quickly and permanently after therapy. All patients in this group responded favorably to treatment; in none of them did progression of the disease occur.

Sixty patients died during the follow-up period, but death was attributable to the neurosyphilis in 2 patients only; cardiovascular syphilis led to death in 2 other patients. In the remaining 56 patients, the cause of death was unrelated to the syphilitic infection. Malignancy was the most frequent cause of death, occurring in 18 patients (32%). The life expectancy of the patients with neurosyphilis was not shortened, as compared with that of the general Canadian population. This unexpected finding, contrasting to many other reports, may be explained by the following factors: 1. Severe cases were not included in this group of outpatients, since these patients were transferred directly to institutions. 2. General medical and social care was given to these patients.

UROLOGY

Urogenital Tuberculosis, Diagnosis and Therapy. E. Ljunggren. Nord. med. 59:897-902 (June 26) 1958 (In Swedish) [Stockholm].

For early diagnosis in renal tuberculosis, tubercle bacilli in the urine are looked for by the guinea-pig test and culture in all cases with extragenital tuberculosis. As tubercle bacilluria is usually accompanied by pyuria, only specimens of urine containing pus cells need to be sent for the guinea-pig test. Total and partial nephrectomy are now less commonly recommended because of the good results achieved in renal tuberculosis with chemotherapy. Indications for removal of a tuberculous kidney are cement kidney, tuberculous pyonephrosis, and severely impaired function when there is, as a rule, advanced tuberculosis. The best results of chemotherapy of urogenital tuberculosis are attained with a triple-drug treatment (aminosalicylic acid, streptomycin, and isoniazid), always combined with sanatorium treatment. Triple-drug treatment is now the standard method of treatment. The importance of sanatorium treatment has not been lessened by chemotherapy, and it should last at least a year. In case of intolerance or resistance to one of the preparations, the author has continued with the other two preparations, sometimes adding Conteben. Reversion occurred in the 25 cases in which the triple-drug treatment was applied for at least a year, and the guinea-pig test has been negative after ended treatment. The duration of after-observation has averaged 6½ months; should the guinea-pig test become positive after long-continued chemotherapy, this would usually occur within the first months after ended treatment. Maintained recovery is looked for in the majority of the patients treated. Chemotherapeutics are bacteriostatics; the defense powers of the organism must conquer the invading bacilli, and there is no better method to support this process than sanatorium treatment. With sanatorium care the patient is also under constant control with regard to the toxicity of the agents employed. Furthermore, ureter strictures can occur during chemotherapy and destroy the result of the treatment unless there is timely surgical intervention.

Experiences with the Kolff Twin Coil Artificial Kidney. J. H. Holmes, O. G. Stonington, P. Van Schoonhoven, T. W. Richey and Y. Takeda. J. Urol. 80:102-109 (Aug.) 1958 [Baltimore].

The authors report on 93 dialyses performed with the Kolff twin-coil artificial kidney on 62 patients at the University of Colorado School of Medicine from August, 1956, to August, 1957. The oldest patient treated by dialysis was 84 years old, and the youngest was 3½. Of 22 patients with renal failure due to chronic renal disease, 11 died, and 11 were discharged with improvement. The average age of those who died was 42 years and of those who survived 35. Of 23 patients with acute renal failure, 13 died, and 10 survived. The average age of those who survived was 42 years and of those who died 47. Eight patients were dialyzed for acute renal failure due to toxins. Of these, 7 survived, and 1 died. Of 9 patients with barbiturate poisoning, 8 survived, and 1 died of respiratory failure. Dialysis produced prompt and excellent results in most of the patients. Two patients who

were each dialyzed 3 times survived. Two patients were dialyzed 5 times, and in both of them the renal lesion at autopsy was considered irreversible. Multiple dialyses are clinically feasible, and there is no increased risk. The principal indications for dialysis are uremia, electrolyte and fluid imbalance, edema, hyperpotassemia, and intoxication with diffusible toxins. Hemodialysis has been lifesaving in many cases, but the procedure should be limited to major medical centers which have sufficient personnel and a large experience.

Atypical Acute Nephritis: Clinical Observations in Several Cases. E. Hansen. Ugesk. læger **120**:908-913 (July 10) 1958 (In Danish) [Copenhagen].

The 7 cases of acute nephritis with rapid and benign course described, in 5 men and 2 women, aged from 22 to 52 years, were distinguished from the usual acute glomerulonephritis in that hematuria, edema, and hypertension were absent or slight, while the clinical picture was dominated by a marked but transient albuminuria, pronounced impairment of renal function of apparently the same type as seen in tubular nephropathy, and prolonged polyuria with hyposthenuria and isosthenuria. No relation to any preceding streptococcic infection could be established. The cases are thought to represent a special form of nephritis of unknown etiology. Attention is called to the similarity to the "epidemic nephropathy" reported in Norwegian and Swedish literature.

THERAPEUTICS

The Influence of Anticoagulant Therapy on the Occurrence of Cardiac Rupture and Hemopericardium Following Heart Infarction: I. A Study of 89 Cases of Hemopericardium (81 of Them Cardiac Rupture). S. Aarseth and H. F. Lange. Am. Heart J. **56**:250-256 (Aug.) 1958 [St. Louis].

The present study is concerned with 89 (7.3%) cases of hemopericardium found at autopsy in a series of 1,303 patients who died of heart infarction. Of these 5 had hemopericardium without rupture, and 3 had rupture of the ascending aorta, while the remaining 81 cases had myocardial rupture. The 41 men were aged 41 to 86 years with a mean of 68.5 years, the 48 women ranging in age from 55 to 90 years with a mean age of 72.5 years. The greatest number of instances of hemopericardium with myocardial or aortic rupture were found in the 60-to-79-year age group, the males predominating in the under 60 group, and a greater number of females being present in the group past the age of 80. Twenty-nine patients had a history of previous angina pectoris, 3 had had previous infarctions, 46 had not had symptoms of angina pectoris, and in 8 cases adequate information was not obtained. Hypertension was not uncommon, 33 patients having systolic pressures in excess of 160 mm. Hg and 20 having diastolic pressures above 100 mm. Hg. Aortic stenosis was present in 6 patients, 1 of whom had mitral stenosis as well, syphilitic aortitis in 1, and inveterate syphilis in 1. Serologic tests carried out in 57 of the patients including the 2 mentioned above were negative in all instances. Seven patients (7.6%) had diabetes mellitus.

A study of height-weight ratios did not reveal any particular relation between overweight and cardiac rupture. Anticoagulant therapy was given 33 (37%) of the patients. Hemopericardium without rupture of the heart or aorta was restricted to the latter group, which also included 8 patients who had excessive anticoagulant effect shortly before death. The figures regarding the clinical duration of the infarct, i. e., the interval between infarction and rupture (death), are not considered reliable. More than half the cases died during the first 5 days and about 80% (73) died during the first 10 days, 22 of the 33 receiving anticoagulant therapy dying during a period from the fourth to the ninth day. The rupture was of the left ventricle in all of the 81 cases, and in most instances was near the apex, involving the anterior wall in 43 instances and the posterior wall in 29. The size of the rupture varied from an opening barely admitting a thin probe to tears up to 4 cm. in length. Coronary lesions were demonstrated in several instances as was cardiac hypertrophy. The authors conclude that a fatal hemopericardium may occasionally be caused by anticoagulant therapy in myocardial infarction even in patients within a safe range of anticoagulant effect. A number of cases with excessive anticoagulant effect sustained cardiac rupture, and in these cases an overdose of anticoagulant or excessive anticoagulant effect seems to have precipitated a fatal cardiac rupture.

The Influence of Anticoagulant Therapy on the Occurrence of Cardiac Rupture and Hemopericardium Following Heart Infarction: II. A Controlled Study of a Selected Treated Group Based on 1,044 Autopsies. H. F. Lange and S. Aarseth. Am. Heart. J. **56**:257-263 (Aug.) 1958 [St. Louis].

Recent observations indicate that anticoagulant therapy in patients with acute myocardial infarction increases the risk of death from rupture or hemopericardium. The primary series which is comprised of a total of 1,044 autopsied cases included patients receiving anticoagulant therapy as well as patients receiving no anticoagulant therapy. The following categories of cases were excluded in both the treated and untreated groups: (1) patients in whom the infarct had not been diagnosed during life, and who consequently had received no anticoagulant; (2) patients showing old infarction; (3)

patients in whom the exact time of infarction was not definitely known; and (4) patients who died before reaching the therapeutic range of anticoagulant effect. The treated group consisted of 40 men and 29 women, and the untreated group (control) of 38 men and 34 women. The average age for men was 65.3 years in the treated group, and 66.1 in the control group, while the average age for women was 74.8 and 75.5 years respectively. None of the women were less than 60 years of age, the male-female age difference being 9.5 years in the treated group and 9.4 years in the control group. Seventy per cent of the deaths in the treated group and 64% of the deaths in the control group occurred within 20 days after infarction. Although 50% of the patients in the control group died within 5 to 9 days there was a greater variation in the length of survival in the treated group, which was ascribed to the routine discontinuance of anticoagulant therapy after 4 weeks and was attended by an immediate rise in temperature and subsequent death in a number of patients. There was only 1 instance of hemopericardium without rupture. Hemorrhagic fluid with or without fibrin deposits was found in 10 patients in the treated group (14.5%), and in 4 patients in the control group (5.5%), while serous fluid was found in 8 patients (11.6%) of the treated group and in 18 patients (25%) of control group. Normal pericardium was noted in 22 (32%) of the treated group and in 31 (43%) of the control group. Intracardiac mural thrombi were found less frequently in the treated group (6%) than in the control group (11%). The incidence of hemopericardium in the treated group was almost twice as large (15 of 69 patients) as in the control group (8 of 72 patients), permitting the conclusion that anticoagulant therapy may contribute to the weakening of the affected area of the myocardium with consequent rupture.

Therapy of Choriocarcinoma and Related Trophoblastic Tumors with Folic Acid and Purine Antagonists. Min Chui Li, R. Hertz and D. M. Bergenstal. New England J. Med. 259:66-74 (July 10) 1958 [Boston].

The authors report their experience with the treatment of 6 men and 5 women suffering from choriocarcinoma or related trophoblastic disease, the diagnosis of which was based on unequivocal histological evidence. The patients, all of whom were hospitalized throughout all periods of active therapy, received either orally or intramuscularly a daily dose for 5 consecutive days of 15 to 25 mg. of methotrexate; 6-mercaptopurine was administered orally in daily doses of 600 to 800 mg. for 5 days. No further therapy was given until all signs of induced toxicity had completely subsided, subsequent courses of 5 days' duration being administered with similar precautions. The most sensitive criterion of therapeutic effort was found to be the level of urinary chorionic gonadotropin. In all 6 women the repeated courses of methotrexate administration were followed by unequivocal evidence of tumor regression and a concomitant drop in gonadotropin excretion. The 5 male patients failed to show any distinct response to methotrexate or 6-mercaptopurine, their clinical status remaining unimproved and x-ray examination revealing no decisive retrogression of the extensive metastases. Only minor fluctuations in the gonadotropin titers were noted, the disease process running an unrelenting course with 4 of the 5 men dying with characteristic manifestations of the primary disease. Procedures aimed at rendering the internal environment of the male host more comparable to that of the female failed to alter the tumor response.

Pharmacology and Clinical Use of Pempidine in the Treatment of Hypertension. M. Harington, P. Kincaid-Smith and M. D. Milne. Lancet 2:6-11 (July 5) 1958 [London].

The authors studied a new drug of the amine, ganglion-blocking type. This drug is 1:2:2:6:6-pentamethyl piperidine. It is known under the common name pempidine, and the name "perolysen" has been proposed. Pempidine is a tertiary amine, a simple derivative of piperidine of empirical formula $C_{10}H_{21}N$. For experimental studies on pempidine the same method was used as for mecamylamine. Thirty-two hypertensive patients without renal failure were given pempidine, and of these 27 received continuous treatment. Observations were made on 2 patients with hypertension complicated by moderate uremia. Twenty-one patients were studied after a single intravenous dose of pempidine. In all except 2 cases the drug was given in a dose of 5 mg. of hydrochloride (4 mg. base). Single oral doses of 5 to 20 mg. of bitartrate (2.5-10 mg. pempidine base) were given to 9 patients. A hypotensive effect was usually observed within an hour after an oral dose. The duration of hypotensive action was 6 to 7 hours after the dose, although the maximal effect lasted for only 1 to 3 hours. In 2 cases after an intravenous dose, and in 3 after a large oral dose, there was a severe fall in blood pressure, and the effect of the drug was prolonged for as long as 24 to 36 hours. One of these patients had severe oliguria which undoubtedly interfered with excretion of the drug. In 24 of the 27 patients who received continuous treatment with pempidine treatment had been continued to the time of this report, for from 2 to 20 weeks (average 10 weeks).

Pempidine is similar in many respects to mecamylamine. Both drugs are rapidly and completely absorbed from the intestine. They readily cross

cell memebranes and are concentrated within tissues by intracellular protein-binding, especially to nucleoproteins. The excretion of both drugs is influenced by urinary pH, clearance being decreased in alkaline and slightly increased in acid urine. Several differences make pempidine a potentially more useful drug than mecamylamine. While 25% of mecamylamine is bound to plasma-protein, pempidine is not so bound, and therefore all the drug in plasma is pharmacologically active. Pempidine is excreted more rapidly than mecamylamine. This is advantageous because toxic accumulation of the drug in the body is less likely. In addition, the dosage of pempidine can safely be increased to effective levels more rapidly than that of mecamylamine. Excretion of pempidine is less affected by variation in acid-base balance than that of mecamylamine. The difference between an effective and a toxic concentration is probably greater in the case of pempidine. A steady hypotensive effect can be maintained throughout the day when pempidine is given orally at 5-hour intervals. The dosage of pempidine can be quickly increased, owing to the rapid elimination of the drug.

ANESTHESIA

Single Lung Anesthesia in Surgery. I. S. Zhorov. Khirurgiya **34**:11-20 (No. 6) 1958 (In Russian) [Moscow].

Indications for single lung anesthesia are limited. It is employed mainly in total removal of the lung and occasionally in removal of 1 or 2 lobes. Single lung anesthesia has certain advantages over endotracheal anesthesia during operations connected with purulent lung diseases, since it provides the best isolation of the diseased lung from the healthy one and prevents penetration of infected and non-infected masses into the latter. Single lung anesthesia provides sufficient oxygen saturation of the blood. This anesthesia is induced by the block of the main bronchus of the diseased (operated on) lung and by endotracheal anesthesia or by introduction of a tube into the bronchus of the unaffected lung for endobronchial anesthesia. Single lung anesthesia is more complicated than endotracheal, since at times it requires roentgenologic examination besides the physical one. It may be carried out by any experienced anesthesiologist.

Minor Laryngeal Sequelae of Endotracheal Intubation. B. Wolfson. Brit. J. Anaesth. **30**:326-332 (July) 1958 [Altrincham, England].

In an attempt to assess the number of minor laryngeal sequelae produced by intubation in the everyday anesthetic practice of a fairly large hospital, the author interviewed between the 2nd and the 8th postoperative day 521 patients who had been operated on with the aid of endotracheal anesthesia at the Western Infirmary in Glasgow, Scotland. The complaints elicited by the interrogation were as follows: Eighty-three patients (15.9%) had a slight sore throat; 13 (2.5%) had a severe sore throat; 17 (3.3%) were hoarse; 2 (0.4%) lost their voices temporarily; and 4 (0.8%) had sore throats and were also hoarse. The complications lasted from 3 hours to 7 days. Fifty-four patients (10.3%) had complications lasting 2 or more days, and 61 patients (11%) had complications lasting less than 2 days. The incidence was affected only by the sex of the patient, being much greater in the female patients. There was a greater incidence also in patients in the prone position than in the supine, lithotomy, Trendelenburg, or lateral positions, but the figures were not statistically significant.

PUBLIC HEALTH

Killed Antituberculous Vaccine—V. D. S. Vaccine (Diffusing Vaccine Salvioli): V. Clinical, Roentgenologic, and Hematological State (in 1956) of Newborn Infants Vaccinated (in 1954-1955) with V. D. S. Who Were Exposed to Tuberculous Infection in the Family. F. Grandi and M. Malossi. Minerva Med. **49**:2545-2566 (June 27) 1958 (In Italian) [Turin, Italy].

Forty-three infants, most of whom belonged to families in which at least one member had tuberculous disease, were born at a community maternity center and were vaccinated at birth with diffusing vaccine Salvioli (V. D. S.) during the period 1954-1955. A year later 40 of the infants were examined for the possible presence of tuberculous disease, but none had such disease as established by clinical and roentgenologic examinations. Most of the infants presented positive reaction to Wolmer's tuberculin test. The general state of health was satisfactory, although the infants came from poor homes and most of them were bottle-fed. The erythrocyte sedimentation rate tended, on the average, to reach the upper physiological limits. The white blood cell count varied between 9,200 and 24,800 per cubic millimeter, which values exceed the mean physiological value of 10,000 per cubic millimeter according to Lavergne's formula. The leukocytic formula (differential count) did not deviate significantly from the normal values, with the exception of a slight increase in the eosinophil count. The Velez index, which has a high diagnostic value for excluding tuberculous disease where it is not actually present, was negative in all the children. The Arneth-Cooke formula also presented nonpathological values. Vaccination of newborn infants with the killed antituberculous vaccine, V. D. S., has thus been shown to be an innocuous

procedure, even if administered to feeble infants living in an environment where they are highly exposed to Mycobacterium tuberculosis. It is not necessary to put the children in preallergic isolation.

Killed Antituberculous Vaccine—V. D. S. Vaccine (Diffusing Vaccine Salvioli): VI. Reexamination (in 1957) a Year After Initial Examination (in 1956) of a Group of Infants Who Were Vaccinated at Birth with V. D. S. and Exposed to Tuberculous Infection in the Family. F. Grandi and M. Malossi. Minerva med. 49:2566-2575 (June 27) 1958 (In Italian) [Turin, Italy].

In 1957 a second clinical and roentgenologic inspection was made a year after the initial study in a group of 30 infants who were vaccinated at birth with diffusing vaccine Salvioli (V. D. S.). Tuberculous disease was known to exist in the homes of 20 infants and was presumed to be present in the homes of the others. The leukocytic formula (differential count), Arneth-Cooke formula, Velez index, and Wolmer tuberculin test were investigated in all the infants. All the children but one were free of the clinical symptoms of tuberculous disease. Body weight had increased in 27 infants. Sensitivity to tuberculin, as evidenced by the reaction to the Wolmer test, increased in 8 infants, remained unchanged in 8, and decreased in 13, as compared with the reaction to the test in 1956. The Velez index, which was negative in all but one infant, was, on the average, more negative than the year before.

The primary phase of a tuberculous process of exudative type was established in the one infant who was ill. The disease, which had taken a mild form, was easily controlled and cured with chemotherapy, since there were few local symptoms and the absence of such general symptoms as fever affected the child's well-being and body weight. The case demonstrated the efficacy of the V. D. S. vaccine in mobilizing antibodies for attacking the etiological agent of tuberculosis in infants. The infant was again examined a year after remission of the disease and was found to be healthy. This second examination once again demonstrated the effectiveness of the V. D. S. vaccine in protecting vaccinated infants against tuberculous disease during the first 2 or 3 years of life despite poor economic and hygienic conditions.

Field and Laboratory Studies on Equine Encephalitis. R. F. Feemster, R. E. Wheeler, J. B. Daniels and others. New England J. Med. 259:107-113 (July 17) 1958 [Boston].

Research activities have been carried out in the state of Massachusetts since 1938 to determine the possible reservoirs and vectors of the virus of equine encephalitis. At the time of the outbreak in horses and human beings in 1938 the only known laboratory vectors of the equine viruses were 8 species of mosquitoes belonging to the Aedes genus. In 1941 Hammon and co-workers isolated the western equine virus from free-living mosquitoes of the Culex genus, thus proving that transmission was not restricted to the Aedes genus. In 1943 the same group demonstrated that barnyard fowl could act as reservoirs of the St. Louis and the Western equine-types of encephalitis. In 1953 a total of 146 specimens of blood were obtained from birds shot in the vicinity of Hockomock swamp, which is located near the communities of Easton, West Bridgewater, Bridgewater, Raynham, Tauton, and Norton. In addition, blood specimens from 19 horses were collected. Of the latter group, 1 had antibodies for the eastern virus of equine encephalitis alone, 6 for the western virus alone, and 2 for both. A total of 105 (71.8%) of the 146 birds had no antibodies for the eastern virus, 8 (5.5%) not having been tested for such antibodies, and only the last bird shot in the study yielded the eastern virus by isolation. Twenty (13.7%) of the birds gave evidence of infection with the eastern virus alone, 2 (1.4%) with the western virus alone, and 13 (8.9%) with both.

Late in 1955, after 44 horses had become infected, 4 human cases of equine encephalitis were reported in Boston hospitals, 1 of which was fatal. Four pheasant farms had losses owing to the virus, and 2 pheasants, found ill in the field, yielded the eastern virus. Only 2 of the 356 persons living in close proximity to the Hockomock swamp, from whom blood specimens were taken in 1956, gave positive neutralization tests for the eastern virus, with indexes of 32 and 80 respectively. An additional survey revealed that, of a total of 537 persons with no history of encephalitis, 3 (0.7%) showed low titers of neutralizing antibodies, indicating that inapparent infections with the eastern equine virus in Massachusetts are so infrequent as to be of little significance. Another survey of 152 birds in 1956 revealed 55 birds with evidence of infection with the eastern virus, while 12 had been infected with both the St. Louis and the eastern equine viruses. The eastern virus was isolated from 4 birds; only 4 birds showed antibodies for the St. Louis virus alone. Of the 269 birds studied in the 1957 series, only 12 had antibodies for the eastern virus of equine encephalitis, 9 of them being crows. Four chickens out of 85 tested and 5 turkeys out of 66 tested showed antibodies for the eastern virus. It is of note that 7 out of 39 pigs tested had antibodies for this same virus of equine encephalitis. Culiseta melanura is the mosquito that has been indicated as the vector among birds, and perhaps as the vector from bird to man and horse, while wild birds appear to be the reservoir of the disease for both man and horse.

BOOK REVIEWS

Intestinal Obstruction. By Claude E. Welch, M.D., D.Sci., Clinical Associate in Surgery, Harvard Medical School, Boston. Cloth. $10.50. Pp. 376, with 135 illustrations, drawings by Muriel McLatchie Miller. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, 1958.

From the mass of literature on intestinal obstruction and from his own experiences, the author has presented the salient facts about intestinal obstruction. This monograph is thus a ready reference for interns, residents, and surgeons who are responsible for the care of such patients. In the early chapters, the causative factors, lesions, and pathological physiology are reviewed as an introduction to the clinical management of patients with intestinal obstructions. In the discussion of the diagnosis of intestinal obstruction, it is wisely stated that "although the diagnosis can be made by x-ray, in 90% of the cases strict reliance on this method is unwise." Close cooperation between radiologist and surgeon is necessary to obtain the best result. Although the danger of giving barium to patients with intestinal obstruction is fully discussed, the author is not opposed to giving thin barium or sodium acetrizoate orally in order to locate the site of an obstruction of the small intestine. Intestinal intubation and the general problem of replacement therapy are thoroughly discussed. Because of the danger of intestinal strangulation during prolonged unsuccessful intestinal intubation, the author advises early operation in simple types of obstruction. The major part of the book is devoted to the management of the various types of intestinal obstruction. Each type is discussed from the standpoint of etiology, symptoms, diagnosis, and treatment. The author's surgical technique is well and profusely illustrated. The many causes of postoperative obstruction, diagnosis, and their treatment are reviewed. The book has a provocative chapter on intestinal obstruction and peritonitis. The author is inclined to operate on patients with obstruction in the presence of peritonitis when the generally accepted conservative therapy seems to fail. He supports his views with the excellent results in a small series of patients on whom he carried out the lysis of adhesions, intestinal resection and anastomosis, and enterocolostomy in the presence of peritonitis. This monograph is highly recommended to all medical personnel responsible for the care of patients with acute intestinal obstruction.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Law and Ethics for Doctors, with a Section on General Practice in the National Health Service. By Stephen J. Hadfield, M.A., M.B., B.Chir. With contributed sections on negligence by W. G. Hawkins and the late W. Mair. Superannuation by L. S. Potter, M.D., Ch.B. Income tax by W. Donald, C.A. Cloth. 42 shillings. Pp. 399. Eyre & Spottiswoode (Publishers) Ltd., 15 Bedford St., Strand, London, W. C. 2, England, 1958.

This book describes rather fully many of the obligations imposed on the physicians of England by the National Health Service and related acts. It is clearly a handbook to be used by the physician in England who practices his profession in a somewhat less than free climate of medical enterprise. Of general interest, however, is the description of the Privy Council, the General Medical Council, and the Medical Register. Ethical principles are discussed briefly. For members of the medical profession in the United States this book has little practical value. It is, however, a revealing collection of miscellaneous information which indicates all too clearly the regimentation of medical practice under the National Health Service.

The American Academy of Orthopædic Surgeons Instructional Course Lectures. Volume XIV. Editor: R. Beverly Raney, M.D. Cloth. Pp. 388, with illustrations. J. W. Edwards, Ann Arbor, Mich., 1957.

This new volume presents some of the lectures that were given before the American Academy of Orthopædic Surgeons in February, 1957. It is another excellent book in their annual series. It will be of value as a teaching and reference book on the resident level, but it is perhaps too technical for the medical student. Its great value lies in the completeness with which one facet of a surgical problem is handled. This is particularly true in such articles as Congenital Dysplasia and Dislocation of the Hip in Infancy, Proximal Femoral Osteotomies, and Congenital Pseudoarthrosis of the Tibia. There is a wide range of coverage on conditions of the spine and the upper and lower extremities. Of special note are the articles on local manifestations of systemic diseases, or diseases involving the skeleton, which provide interest to the roentgenologist, the pediatrician, and the internist, as well as to the orthopedist. This volume should be read diligently by every young orthopedist intending to take either part of the specialty board examinations. It should be of value also to the older orthopedist, by keeping him abreast of modern trends in operative or orthopedic surgery. No original work or research is reported; the book is a record of the teachings presented at the annual meeting. The articles on

interpretation of pain are nebulous and inclined to give quotations from older authors too much and to show acceptance of their writings with sometimes an implication of finality. The bibliographies after each article are ample, and the authors cover the subjects succinctly and, as a rule, impartially.

Tumors of the Soft Somatic Tissues: A Clinical Treatise. By George T. Pack, M.D., LL.D., F.A.C.S. Associate Professor of Clinical Surgery, Cornell University Medical College, New York, and Irving M. Ariel, M.D., F.A.C.S., Associate Clinical Professor of Surgery, New York Medical College, New York. Cloth. $30. Pp. 820, with 652 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This comprehensive textbook discusses the clinical management of patients with soft somatic tumors in connective tissues, fat, smooth and striated muscle, fascia, synovia, blood and lymph vessels, and nerve tissues. Each tumor type is discussed, and features that differentiate benign from cancerous growths are presented. The monograph reflects the results of treatment in a group practice during 25 years. It contains six sections: (1) history, classification, incidence, hereditary and congenital occurrence, role of trauma and other etiologic factors, and cancerous evolution of a benign growth; (2) techniques of wide local excision and other details of amputation; (3) treatment of specific tumors and tumor-like or preneoplastic proliferations; (4) sarcomas of infants and children, their treatment and results; (5) the principles of therapy of these tumors in such locations as the neck, abdominal wall, buttocks, and retroperitoneum; and (6) therapeutic results and an analysis of the factors that influence prognosis. The chapters in each section document the subject material presented with a substantial bibliography. The book is well written and illustrated. It presents clearly a large amount of practical information on diagnosis and treatment, including the special techniques of surgery for the many tumors arising in the soft somatic tissues. This information is especially valuable to all surgeons, both in diagnosis and in surgical and radiation treatment. Pathologists also should find this book a good source for information about these tumors.

Pediatric Index: A Guide to Symptomatological Diagnosis and Current Management. By Edwin F. Patton, M.D. Cloth. $13.50. Pp. 639, C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

This book presents an alphabetical listing of all pediatric conditions, normal and abnormal. It is similar to Davison's "Compleat Pediatrician" but more comprehensive. There is no arrangement in body systems or any discussion of disease entities other than the exhaustive listing and correlation of signs and symptoms aimed at assisting in the diagnosis and treatment of all manner of problems of childhood. The material is organized into three sections. The first and largest provides an exhaustive indexing of major signs and symptoms, broken down wherever possible into those found in the infant or the older age group. Minor corroborative or differentiating findings are included, and a suggestive diagnosis is offered. The second section lists abnormal conditions, each with exact information required for a definite diagnosis. Wherever appropriate, a list of conditions to be ruled out is given. The latest or best treatment is then outlined. The third section, dealing with special data and technique, is more meager, and one may wonder why the few techniques given were selected to the exclusion of others. The concise information on electrolyte and fluid adjustment, seizures, and antibiotics in this section is excellent. This book should be considered as a diagnostic reference textbook. The material on poisoning is particularly extensive, and the information on orthopedics goes beyond that found in most pediatric textbooks. Much space is devoted to febrile disorders. The well-differentiated headings, the adequate-sized type, and the multiple cross references facilitate the finding of information. This book is intended as an aid to physicians, experienced or inexperienced, in clarifying obscure pediatric diagnoses, preventing oversight of rare conditions, and providing a guide for treatment.

The Organization and Administration of Physical Education. By Edward F. Voltmer, and Arthur A. Esslinger. Third edition. Cloth. $5. Pp. 558. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1958.

The authors place the emphasis on the education in physical education. Exercise and health are important outcomes, but education for fitness, skill and understanding, and personality and character development is the primary goal. Effective organization and administration of the program facilitates the achievement of this objective. The book is based on a study of current problems in physical education. After delineating the place of physical education in education and outlining aims, the authors emphasize the need for well-defined administrative policies and the means of establishing these. They then show how such policies can be applied in the organization and conduct of the class program in physical education, the intramural sports program, and the program of interscholastic athletics. Equipment and facilities, tests and measurements, budget making and financing, public relations, legal liability, and working with staff members and student leaders are also discussed. Recognizing that school health education may be administered separately from physical education in many school organizations, the authors give it only brief coverage. References are relied on to provide

details for those having dual responsibility or concern for school health education. Through extensive revision, the authors have made the material in this new edition more applicable for a wider audience, including teachers and leaders in service as well as those preparing for teaching and administration of physical education.

General Pathology Based on Lectures Delivered at the Sir William Dunn School of Pathology, University of Oxford. Edited by Sir Howard Florey, Professor of Pathology, University of Oxford, Oxford. Second edition. Cloth. $16. Pp. 932, with 344 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

This book is based on a series of lectures in general pathology and bacteriology given to medical students after completion of their physiology and biochemistry courses and just preceding their clinical work. Stress is laid on the fundamental changes that take place in the body in response to injury. Present-day views about the nature of those changes are discussed. An effort is made to stimulate in the mind of the student an experimental outlook for clinical medicine and surgery. This second edition has been revised and rearranged, and additional chapters on thrombosis, metabolic changes after injury, atherosclerosis, and tumors have been added to make the book more complete. Fourteen authors, in addition to the editor, have contributed special chapters. The authors' aims have been well accomplished, and there is excellent coverage of all aspects of general pathology and bacteriology. The altered physiology in anatomic pathological changes is considered in detail. The historical approach is maintained throughout, and a good background is provided for each subject. Experimental evidence is given in many instances, and throughout the book are numerous excellent photographs and drawings, including color plates. The book is well bound, clearly printed, and easy to read. The European spelling of certain words is interesting but not a detraction. The wealth of detail presented may be more than is desired by many students, but it helps to give an interesting, well-rounded approach to the subject. This book can be recommended to medical students, especially those whose interests extend beyond their required courses in pathology.

A Text on Systemic Pathology. Volume 1. Edited by Otto Saphir, M.D., Director, Department of Pathology, Michael Reese Hospital, Chicago. Cloth. $32. Pp. 865, with 818 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

Pathologists and others often need information pertaining to a disease only to find that the available textbooks fail to go into sufficient detail or sketchily outline the correlation of the clinical findings with the pathologic process. This book, the first of two volumes, was written to fill this vacuum. It takes into account at all times the fact that a diseased organ or organ system is not a separate entity but part of the whole organism. In most instances, the description of a pathological entity begins with the first signs and symptoms, continues through the gross, microscopic, and statistical data, and includes postoperative complications. In addition to the editor, contributors include Maurice Lev, Jay J. Gold, and Ira Gore. The excellent continuity makes for easy reading. The material is presented in a manner which makes the book equally valuable to the pathologist and the nonpathologist and represents the authors' firsthand experience with the subjects discussed, including the findings in a number of diseases which they have studied extensively. The literature has been critically evaluated, and an attempt has been made to eliminate some time-honored opinions which do not stand the test of more recent experience. The photographs are excellent. This book would be a valuable addition to the library of any physician.

Advances in Electrocardiography. Edited by Charles E. Kossmann, B.S., M.D., Med.Sc.D., Associate Professor of Medicine, New York University College of Medicine, New York. Cloth. $9.75. Pp. 280, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This monograph deals with the fundamental advances in electrocardiography made in the period 1946-1956. The editor is assisted by five contributors. The subject matter is discussed under four categories: source of potential, conducting medium, spread of excitation, and recovery and rhythms. Much of the material consists of biochemical, biophysical, and mathematical concepts which form the bases for modern clinical electrocardiography. This portion is written in an interesting manner, is well documented with diagrams and illustrations, and of necessity is not light reading. Other portions deal with fundamental bases of practical electrocardiography and are magnificently presented and illustrated. Of particular note in this latter category are the chapters on intraventricular conduction and electrocardiographic interpretation in congenital heart disease. The purpose of the monograph is to present the most significant advances in the fundamental sciences applied to electrocardiography for the clinician and not to present another textbook on interpretation. The authors have succeeded in their purpose and have fulfilled a great need of the clinician in collecting and correlating the important experimental work from the mountainous mass of published data. This monograph should be in every internist's library.

QUESTIONS AND ANSWERS

ETIOLOGY OF MENTAL DEFICIENCY

To the Editor:—*Please give a summary of the present concept of the relative importance of the various etiological factors in mental deficiency of school-aged children. What is the importance of genetic factors in cases not associated with cerebral palsy?*

Lawrence M. Herman, M.D.
Monterey Park, Calif.

Answer.—It is, perhaps, still helpful to think of the causes of mental deficiency as falling into roughly two large groups—those determined largely by genetic or endogenous factors and those due to exogenous factors related to the environment and its modification during intrauterine or postnatal life. From a clinical standpoint, by far the most types fall into the exogenous group. At the present time this is also the group about which medicine can do much in the way of prevention. Attention to such prenatal factors as infection (via German measles), isoimmunization (**Rh** factor), and toxemias of pregnancy or pelvic irradiation is most important in prevention. Any perinatal factor leading to hypoxia or intracranial hemorrhage and postnatal factors such as encephalitis (primary or allergic), such toxic substances as lead or drug ingestion, severe emotional deprivation in infancy, and severe repeated or prolonged convulsions are factors that physicians can also do much to control or modify. Genetic factors can be thought of from a clinical point of view as due to single recessive genes or to single dominant genes. The clinical pictures in the former group are usually easily recognized, often because the defect is sharply segregated to a family group. Examples of these conditions would be phenylketonuria and galactosuria, both of which can now be detected in infancy, and much damage to the brain can be prevented by appropriate treatment. Other clinical entities of this group are amaurotic idiocies (Tay Sach group) and lipochondrodystrophy (gargoylism), not modifiable at present by treatment. The clinical entities due to single dominant genes are not always so easily identified because of the frequent occurrence of atypical or incomplete form. Tuberous sclerosis and certain of the dysostoses are examples of this group. Many children who are thought to be mentally retarded because of an inability to cope with school work turn out to be children who are educationally handicapped by various forms of brain damage in the areas concerned with the use of symbols. Careful examination by an experienced neurologist, speech therapist, or child psychiatrist often reveals mixed forms of aphasia, agnosia, and apraxia. The importance of recognizing these clinical conditions is that remedial help can be obtained, usually from a skilled speech therapist. These children are not really mentally retarded, but they are educationally retarded because of their great handicaps in learning via the usual symbolic tools. The IQ as a measure of intellectual potential can vary widely in an individual's lifetime, and a single measurement should not be taken as a complete diagnosis—a practice which is unfortunately rather widespread. Every effort should be made to make a diagnosis of retardation based on etiology, i. e., a medical diagnosis.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

MUSCULAR DYSTROPHY

To the Editor:—*An 8-year-old boy who is mentally deficient has developed muscular dystrophy of the pseudohypertrophic type. This disease developed insidiously after a mild case of poliomyelitis in 1955. His history is noncontributory except for a cerebral concussion, in February, 1956, and a large hiatus hernia found at birth. Norethandrolone used empirically in moderate doses apparently increases muscle tone and energy in this child. Please give information concerning the use of this or any other drug helpful in the treatment of this disease. Have any cases of muscular dystrophy in any way correlated with severe head injuries or poliomyelitis been reported?*

George M. Wolverton, M.D., Clarksville, Ind.

Answer.—The child referred to in this question certainly has an unusual complication or collection of neurological conditions—mental deficiency, muscular dystrophy, cerebellar concussion, and poliomyelitis. One certainly must wonder about diagnosis in this case. There is no evidence that muscular dystrophy can in any way be correlated with severe head injuries or that it may develop after poliomyelitis. Were it not for the reported pseudohypertrophy, one would wonder whether his weakness might not be a poliomyelitic residual. No drugs of proved value in muscular dystrophy are available. Vitamins and amino acids have been reported to be of therapeutic value, but controlled studies have failed to confirm this. Norethandrolone should not be given for any prolonged period of time, especially in prepuberal children.

ITCHING OF THE TONGUE

To the Editor:—*A 9-year-old boy complains of his tongue itching. It is not sore or tender, but he takes his fingers to scratch it and it annoys him greatly. This has occurred on and off for three years. It may last for days at a time, or he may be free of the itch for months; it has occurred in any season. The tongue appears normal or has red raised bumps on it. Antihistamines did not help. Please give advice on this problem.*

M.D., Ohio.

Answer.—Itching of the tongue, if it can occur, must be extremely rare. In experiences over a period of 35 years with patients with allergies, including many who have had itching of the palate, this consultant has never encountered an instance of itching of the tongue. The failure to obtain any relief from antihistamines makes it likely that the complaint is not based on a histamine mediation mechanism. The explanation for this complaint is not obvious, but a trial of a tranquilizer, such as hydroxyzine hydrochloride in 10-mg. doses, is suggested.

LOSS OF SMELL AFTER HEAD INJURY

To the Editor:—*A head injury after an automobile accident has caused the loss of smell and a partial loss of taste. The patient is 6 months old. Will this be a permanent condition?*

J. W. Geiger, M.D., LaSalle, Ill.

Answer.—Loss of smell is not an unusual sequel of head injuries. Fracture of the cribriform plate of the ethmoid bone or hemorrhage at the base of the frontal lobes may cause tearing, crushing, or compressing of the olfactory filaments. With such anosomia there is also some loss of ability to perceive and recognize flavors which involve not only taste but also olfactory sensation. Such loss of smell and impairment of taste is often a permanent condition, especially if there has been tearing of the olfactory filaments, and, if there has been no return of function after six months, it may be presumed to be permanent.

ALOPECIA WITH MULTIPLE SCLEROSIS

To the Editor:—*A 39-year-old man, who has had multiple sclerosis for the past five years, complains of spotty loss of his beard. He does not have evidence of alopecia of the scalp. How often does this condition occur? Is it ever associated with multiple sclerosis?*

K. McMorrow, M.D., Detroit.

Answer.—The probable diagnosis of this condition is alopecia areata, a rather common entity. This may be confined to the bearded area. Its etiology is unknown, but psychosomatic influences seem to be important in its causation and in the precipitation of attacks. Alopecia of this type is nonspecific, but there is no reason why it could not occur in association with multiple sclerosis, since psychiatric complications are not unusual in that disease.

HIATUS HERNIA AND PAROXYSMAL TACHYCARDIA

To the Editor:—*Can hiatus hernia cause paroxysmal tachycardia for 31 years? A 52-year-old man has had paroxysmal attacks of supraventricular tachycardia for 31 years. He is sensitive to quinidine and has been responding well to lanatoside C. But, lately, he has been having very frequent attacks. A fairly thorough examination was done, and the only positive finding was a fairly big, sliding hiatus hernia.*

Antonio D. Talusan, M.D., Baltimore, Md.

Answer.—If the hiatus hernia was as big 31 years ago as it is now, then it is feasible that it may be the cause for the tachycardia, through stimulation of the thoracic sympathetic chain. If so, repair of the hernia would be advisable.

XANTHOMA DIABETICORUM

To the Editor:—*Please advise regarding treatment of xanthoma diabeticorum. A 53-year-old woman has numerous lesions on the posterior aspect of elbows, anterior aspect of both knees, and both feet. She is from a family of diabetic persons, but diabetes is controlled in her own case by therapy with 20 units of insulin daily.*

Paul Beddoe, M.D., Alhambra, Cal.

Answer.—Unfortunately there is no satisfactory treatment of xanthoma diabeticorum. The small lesions may sometimes be surgically excised. It is also true that in any of those cases where diabetes is present the treatment of the diabetes does not necessarily affect a resolution of the xanthomatous infiltrations.

BACTERIOPHAGE TREATMENT OF STAPHYLOCOCCIC INFECTIONS

To the Editor:—*What is the presently accepted opinion on bacteriophage treatment of localized or systemic staphylococcic infections?*

M.D., Florida.

Answer.—There have been extensive studies of bacteriophages. When these were discovered, there was great hope that they would serve therapeutically as an effective antibacterial weapon. This has never been realized. Today there is no practical method of employing bacteriophage therapy in the treatment of staphylococcic infections.

DROWNING

To the Editor:—*A local rescue squad has asked for information about the length of time which a drowning victim may remain submerged with hope of recovery. In other words, how long may a person be under water and still be resuscitated by pulmotor or other means? This question is asked to establish a policy for the use of the rescue squad in future drowning incidents.*

Tom Roe, M.D., Savannah, Tenn.

Answer.—The question is best answered in terms of probability. The following table gives percentages based on data supplied originally by A. Keith and quoted in the book "Adventures in Artificial Respiration" (Karpovich, New York, Association Press, 1953, pp. 258-261):

Time Under Water, Min.	Probability of Survival, %	Cases, No.		
		Total	Saved	Lost
1- 5	95	247	234	13
6-10	81	110	89	21
11-15	54	26	14	12
15+	20	20	4	16

It seems to be useless to search for an account of the longest known submersion followed by successful resuscitation; samples of such accounts are given by Karpovich together with the reasons why they have little value. We know that the longest a person ever held his breath, as reported by Karpovich (p. 108), under the most favorable laboratory conditions (healthy young student, completely relaxed, having overbreathed to the point of alkalosis and having also inhaled oxygen) was 20 minutes and 5 seconds. An excited person who has worked up an oxygen debt by struggling before submersion would be at a disadvantage on every count; the only thing in his favor would be that cold water would induce some hypothermia and thus slow the process of asphyxiation.

UNUSUAL MEDICAL QUESTIONS

The Questions and Answers Department of The Journal *receives many letters describing unusual cases. Some of these are too detailed to be printed in the regular Questions and Answers section. From time to time those that represent apparently new or different clinical syndromes or other interesting medical data will be presented in this section of* The Journal.—Ed.

WHEAL AT TUBERCULIN P. P. D. TEST SITE ASSOCIATED WITH ASTHMATIC ATTACK

To the Editor:—*In 1954, a 28-year-old man developed measles complicated by bronchial pneumonia; this was followed by a penicillin reaction, then erythema nodosum, and, two months later, bronchial asthma. Concurrent with an attack of asthma, a wheal often flares in the area of the forearm where he received an intradermal injection of tuberculin P. P. D. in 1950. Could there be any correlation between the wheal and the asthmatic attacks? Has anyone ever attempted desensitization with tuberculin?*

Harold N. Cooper, M.D., San Antonio, Texas.

Answer.—Since no familial history of allergy is given in this case, the origin of the allergy is more uncertain. It could be either truly allergenic or psychogenic. In the latter case, desensitization with histamine phosphate has been used by some physicians. If this treatment proves ineffective, then a true allergenic origin may be considered. Because of the location of residence, histoplasmin sensitization should be considered and, also, a possible sensitization to a host of other cross-reacting acid-fast organisms. Extensive skin testing with products of such organisms may give a clue as to the origin of the sensitization. Desensitization with tuberculin has been used in humans with suspected ophthalmic tuberculous allergy. However, the benefits versus the harm of desensitization have not so far been adequately evaluated. Recent studies in infected animals show that injection of much tuberculoprotein causes a disappearance of circulating antibodies to the tuberculopolysaccharide, a great extension in caseation, and hastening of death. Injection of tuberculopolysaccharide interferes with complement fixation and other immunological processes and also with the natural bacteriostatic activity of serum.

Answer.—It is a fairly common occurrence for a site previously injected with an antigen to flare up under certain conditions. For example, the injection of an antigen (such as ragweed pollen) in one area may cause a reaction in the other arm where the same antigen or a dissimilar one (such as grass pollen) had been previously injected. It has been noted that such a flare-up can occur when the patient inhales the antigen during the season, and it can also happen as a result of ingestion of an allergenic food or drug. Even exposure to cold (swimming) or to heat, or any other physical upset, such as gastrointestinal or emotional upset, may cause the flare-up. The mechanism of this phenomenon is not clear. A possible explanation is that the site which had previously reacted to an antigen had been conditioned to react to other stimuli so that the cells will respond by releasing histamine or other mediators. Desensitization with tuberculin

is possible but would not be indicated in this case. If the inquirer has not already done so, he should do everything necessary to determine the allergic or other causative factors for the asthma.

ANSWER.—It is not unusual to see individuals who, for months or years after the original tuberculin reaction has subsided, have redness reappear at the site of the former reaction when the skin becomes cold. It has also been observed that, in an occasional person, administration of a tuberculin test in another location may result in temporary changes of the skin at the site of an old previous reaction. These phenomena have never been satisfactorily explained. It seems doubtful that there is any significant correlation between the wheal and the attacks of asthma. Most persons who have reported various phenomena which have occurred at the sites of old tuberculin reactions have had them in association with other conditions than asthma. There has been a large volume of work done on desensitization with tuberculin, in both animals and people. Hypersensitivity to tuberculoprotein causes this protein to become a violent poison to living tissues. Tuberculoprotein may be introduced into nonsensitized tissues in a large amount without harm. However, if tuberculoprotein comes in contact with sensitized tissues, it is so poisonous to the tissues that, if present in sufficient amount, it results in necrosis. Thus, tuberculoprotein liberated from bacilli in lesions of such organs as lungs and kidneys may result in enough necrotic tissue to leave cavities. Koch originally believed that introduction of tuberculin was valuable in treatment in that it resulted in reactions, including hyperemia, at the sites of tuberculous lesions. He thought that this stimulation was helpful in promoting the healing process. However, later observations revealed that it has the opposite effect in many cases, resulting in spread of the disease and, sometimes, in rapid progression of lesions. Koch used large doses of tuberculin, but some workers thought that smaller doses which would result in only slight reaction at the site of the disease would promote healing. It was observed that by repeating injection of the same amount of tuberculin several times there ceased to be evidence of macroscopic reaction. This was thought to be due to development of "tolerance" to tuberculoprotein. Therefore, the dosage was increased, and tolerance appeared with each successive larger dose of tuberculin administered until an amount was tolerated which would have resulted in serious consequences if it had been administered initially. There were those who so clung to the treatment value of tuberculin on the basis of the reaction that it produced, even though microscopic as they suspected, that its use was long continued in the treatment of this disease. Later, it was well established that it did not result in the imaginary microscopic reaction in lesions after administration of tuberculin but, rather, that it desensitized the tissues. This, therefore, was responsible for the so-called tolerance to tuberculin in the absence of both macroscopic and microscopic reactions in the lesions. The belief that hypersensitivity to tuberculoprotein is an asset in the prevention of clinical lesions or in their healing has been replaced by well-documented evidence that it is a liability in both instances. Tuberculin administrations have been employed for desensitization in asthma when it was thought that hypersensitivity to tuberculoprotein was responsible. However, this apparently is a rare cause for asthmatic attacks, and such treatment should be considered only when all other possibilities have been ruled out as far as possible. There is no harm in desensitizing the tissues of the human body with tuberculin, provided that the dosage is kept below the skin-reaction level at all times. If desensitization is achieved, even to such a low level that 10 mg. of tuberculin will not result in a reaction, it can be maintained only by continuous administrations of tuberculin. If this is discontinued, sensitivity of the tissues returns and remains as long as living tubercle bacilli are present in the body under circumstances which permit liberation of sufficient amount of tuberculoprotein to maintain it.

CORAL SNAKE BITES

TO THE EDITOR.—*I have just read in the Questions and Answers section of* THE JOURNAL *a discussion about poisonous snake bites. However, the very one I wanted to know about, that of the coral snake, was omitted. There has recently been found in this vicinity two coral snakes, the identity of which is certain. Please give information on the exact and specific treatment, particularly the antivenin dose, as well as any special supportive measures. There has been some conflicting opinions among some authorities in regard to ACTH and hydrocortisone sodium succinate. Is it, or isn't it, indicated?*

David Eanes, M.D., Temple, Texas.

ANSWER.—Little is known about the venom of the North American coral snakes (Micrurus). Probably no single physician in the United States has had extensive experience in treating their bites. There are no reports in the literature of "large" numbers of cases. Little is known about the frequency of coral snake bites; however, they are probably rare owing to the snakes' limited geographical distribution and their relatively unaggressive behavior. In Florida, a study of the incidence of snake bites showed that only 5 (2%) of 241 poisonous snake bites were inflicted by coral snakes (Parrish, *Am. J. Trop. Med.* 6:761, 1957). This consultant has personally seen and treated four persons with coral snake bites. These bites all consisted of scratches on the skin from the fangs—there was no deep impregnation of

the venom, and no symptoms of venom poisoning developed. These incidents would be classed as "poisonous snake bites without envenomation." No specific treatment was deemed necessary in these cases. The coral snake has very short fangs and usually must "chew" its venom into a human being. Neill reviewed the literature of coral snake bites and reported an additional 21 bites with 4 deaths (*Herpetologica* 13:111, 1957). These cases were investigated by means of a questionnaire. Many of these questionnaires were answered by the family and not by a physician. However, coral snake venom is toxic, and human deaths resulting from coral snake bites have been recorded.

The venom of the coral snake is similar to that of the cobra and is primarily neurotoxic in action. Symptoms include local pain, motor paralysis, muscular twitching, inability to speak clearly, salivation, numbness, and respiratory difficulty. Death usually results from respiratory paralysis. Treatment consists of the usual tourniquet with incision and suction if the bite is seen early. There is a specific antivenin for coral snakes, antielapid antivenin, which is effective for the South American coral snakes (and presumably for the North American coral snakes also). It is manufactured by the Instituto Butantan, Sao Paulo, Brazil. From 10 to 50 cc. is the recommended dose. In general, antivenins for neurotoxic venoms are more effective than antivenins for hematoxic venoms. Note that antivenin (crotalidae) polyvalent, the only snake antivenin manufactured in the United States, is not effective against coral snakes. Other therapy is supportive in nature and is somewhat similar to that used for bulbar poliomyelitis. A tracheotomy, oxygen therapy, and a respirator may tide a patient over respiratory paralysis. Antibiotics and tetanus toxoid and/or antitoxin should be given to prevent infections. Morphine and other narcotics which depress the central nervous system are contraindicated. Central nervous system stimulants, such as nikethamide and caffeine may be tried. Shock should be combated by intravenous administration of blood, plasma, and electrolytes. Cortisone and ACTH do not prevent death in snake venom poisoning but may afford some symptomatic and supportive benefits.

ULCERATIVE COLITIS AND OSTEOPOROSIS

To the Editor:—*A 38-year-old man was recently hospitalized because of an acute compression fracture of T-10. A history of intermittent diarrhea of more than 15 years was obtained. Stools were noted by him as brown, occasionally blood-streaked, and mushy. Roentgenograms revealed ulcerative colitis of the transverse and descending colon and sigmoid, as well as diffuse ileitis involving about 25 cm. of the terminal ileum. The ascending colon and cecum appeared uninvolved. Sigmoidoscopy revealed a granular mucosa in the upper sigmoid only, which on biopsy revealed accumulations of lymph and plasma cells in the mucosa and submucosa with no giant cells, and a diagnosis of nonspecific inflammation was made. Bone survey revealed generalized osteoporosis involving the right femur, tibia, humerus, and spine. There was diffuse demineralization and loss of trabeculation, as well as the compression fracture in the thoracic spine. The lamina dura was present. Laboratory findings included the following data: 24-hour urine calcium level (milk-free diet), 164 mg.; serum alkaline phosphatase level, 5.7 Shinowara (S. J. R.) units; sodium level, 143 mEq. per liter; potassium level, 4.5 mEq. per liter; calcium level, 9.2 mg. %; phosphorus level, 3.5 mg. %; stool fat, negative; prothrombin time, 76%; histamine gastric analysis, total 74 degrees, free acid, 60 degrees; glucose tolerance curve, 67, 127, 168, 163, and 72 mg. %; serum carotene 126 I. U. per 100 cc.; thymol turbidity, 3.5 units; sulfobromophthalein, 4.5%; stool guaiac, 1+; serum protein-bound iodine level, 5.5 mcg. %; urea nitrogen level, 11 mg. %; protein albumin and globulin levels, 3.2 and 4.6 Gm.%; hemoglobin level, 14.8 Gm.%; and white blood cell count, 8,650 per cubic millimeter. Could osteoporosis occur secondary to ileitis in this case, with normal serum calcium, phosphorus, and alkaline phosphatase levels? Do abnormal findings on tolerance tests (carotene, glucose) revert to normal in quiescent intervals? Does the absence of gross fat in the stool rule out marked steatorrhea of a degree necessary to produce this picture, or would fat partitions and balance tests of nitrogen aid in the diagnosis? Is folic acid, vitamin B_{12}, or liver therapy useful if there is no anemia or achlorhydria? Is steroid therapy indicated to increase calcium absorption?*

Leonard Breslaw, M.D., Los Angeles.

Answer.—The record of this patient contains several unusual features. The segmental ulcerative colitis of the transverse colon with a normal ascending colon and then diffuse ileitis of such a long stretch of ileum is rare. The physical examination and the laboratory data indicate the patient's condition to be rather good. Osteoporosis secondary to an extensive ileitis is possible, but certainly one would expect changes in the calcium and phosphorus levels of the serum. Abnormal findings on tolerance tests may revert to normal when the intestinal condition is quiescent. The absence of gross fat in the stools indicates the absence of a steatorrhea of any marked degree. Further investigations for the cause of the so-called osteoporosis and fracture of the thoracic spine should be undertaken. The possibility of metastatic malignancy might be considered. Folic acid, vitamin B_{12}, or liver would hardly be indicated in a patient with such satisfactory laboratory data. The advisability of the use of steroids is questionable. The case is unusual and warrants further study.